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The University of Arizona, 1992

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A Patient / Therapist Interactive Feedback Control System to Regulate Temperature and Control Pain in Scanned Focused Ultrasound Hyperthermia

by

Scott Mitchell Nathanson

A Masters Thesis Submitted to the Faculty of the
DEPARTMENT OF AEROSPACE AND MECHANICAL ENGINEERING
In partial Fulfillment of the Requirements
For the Degree of
MASTERS OF SCIENCE
In the Graduate College
THE UNIVERSITY OF ARIZONA

1992

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This thesis has been approved on the date shown below:

_____ _____

R. B. Roemer
Professor of Mechanical Engineering

1/27/92
Date

DEDICATION

This thesis is dedicated to bureaucracy and all the people who made this task almost impossible.

ACKNOWLEDGMENT

I would like to thank everyone who made this work possible. First, Dr. Robert Roemer for his initial encouragement and then his continual belief that I was capable of this task. Dr. Kullervo Hynynen for his many ideas, valuable suggestions, and the key phrase "It is easy". Dr. Hal Tharp for teaching me how to control the world (feedback not dictatorship). Dennis Anhalt for his much needed technical assistance and his reminders to everyone that "It just doesn't matter". Mark Buchanan for his practical engineering knowledge and for his ability to suggest ideas that added many pages to this document. I only hope that one day I am able to pay him back. Andy Dutton for friendship and the continual reminders of what life is like with stress. Eugene Gross, who with a simple suggestion will solve all of your technical problems. Without Eugene, no one would graduate. It is hoped that one day soon we may all call him Doctor. Matt Rademacher who has the ability to take life's ordinary events and make them into "Matt adventures". His adventures are worthy of a major motion picture that would make Indiana Jones seem like a geriatric documentary. David Lamden for his life long friendship and expert proofreading abilities. And The Big A for a never ending supply of onion rings that would make Exxon cry. But most of all I would like to thank my parents who not only gave me the strength to press on but made me possible.

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ABSTRACT

An interactive temperature and patient pain feedback controller with manual power control as a function of scan position has been developed and clinically implemented in treating cancerous tumors utilizing the University of Arizona Cancer Center's Scanned Focused Ultrasound Hyperthermia system. The temperature controller implemented uses a Bang-Bang PID controller in 12 adjacent regions. The controller is shown to be able to reduce unwanted hot spots without substantially increasing the size of cold spots in the treatment volume. The addition of patient feedback during treatments has reduced the frequency of undesirable treatment modifications such as moving the scan or lowering of ultrasound power. Patients were able to repeatedly indicate the areas of pain with a pain button during treatments allowing a computer to determine the maximum tolerable power without excessive discomfort.

CHAPTER 1.0: INTRODUCTION

1.1 HYPERTHERMIA AND SCANNED FOCUSED ULTRASOUND

Modern use of hyperthermia in the treatment of cancer began in the late 1800's when Coley noted that the introduction of bacterial toxins had a therapeutic effect in the treatment of inoperable round cell sarcomas of the neck (Miller et al. 1977). It was not known at the time whether the toxins or the resulting high fevers were the source of the improvements in the cancers. Fortunately for the hyperthermia field, it was soon realized that it was the fever that was the source of the beneficial results. Fever therapy was then used for a wide variety of ailments including infectious diseases and even arthritis (Miller et al. 1977). Since that time, many different modalities have been utilized for inducing hyperthermia. Methods that heat large areas of the body include hot water emersion (Overgaard 1980), convective ovens, heating from magnetic induction by the use of helical coils (Oleson 1984) and microwave antenna arrays (Herman et al. 1988). Techniques for site specific temperature elevation include the implantation of ferromagnetic seeds (Stauffer et al. 1984), interstitial microwaves (Trembly et al. 1896), radio frequency current (Dewhirst et al. 1982), and external ultrasound (Marmor et al. 1979, Lele 1983) and intracavitary ultrasound (Diederich and Hynynen 1989). The use of ultrasound as a means to treat cancer began over 50 years ago with research falling into one of three categories; ultrasound alone, ultrasound in combination with radiotherapy, and ultrasound in combination with chemotherapy. In a survey by

Overgaard 1989, hyperthermia was found to be most effective when combined with radiotherapy. In the opinion of the author, the optimal technique is dependent on the size and location of the site to be treated. Because of the wide variety of sites and locations that are seen in patients, the flexibility of ultrasound has shown great promise in recent years (Harari et al. 1991, Hynynen et al. 1987, Lele 1975, Shimm et al. 1988). Ultrasound's flexibility stems from its ability to provide variable power deposition patterns through techniques such as focusing and/or scanning (Hynynen and Lulu, 1990) allowing for sufficient power deposition to induce therapeutic temperatures in tissue. However, the flexibility of ultrasound also makes it difficult to use. Currently, one of the limiting factors on the further use of ultrasound is the present state of the technology being used. One of the areas that needs improvement is temperature feedback control of the ultrasound power because the existing controllers do not adequately deal with the various conditions and disturbances that are present in the human body. Another limiting factor in hyperthermia treatments that needs attention is the ability to eliminate and/or reduce patient pain. This work was undertaken in order to improve the operation of Scanned Focused Ultrasound (SFUS) in both of these areas.

1.2 THE NEED FOR IMPROVED TEMPERATURE CONTROL

The theoretical goal of a hyperthermia treatment (Roemer, 1991) is to elevate the tumorous tissue region to a target temperature while leaving the surrounding normal tissue temperature unchanged. With this goal in mind, a measure of the success of a clinical

SFUS hyperthermia treatment can be made by looking at what percentage of the temperature probes in the target volume are above a therapeutic target temperature e.g. 42.5 °C. Also, it has been established that there is a link between the minimum measured temperature and the effectiveness of a treatment when only a few sensors are monitored (Dewhirst and Sim 1984). Additionally, high temperatures can be destructive to normal healthy tissue. It is therefore desirable to avoid high temperatures in normal tissue and avoid low temperatures in the tumor while also attaining a uniform temperature field in the tumor (Roemer 1991). However, as noted by Marmor et al. 1979, achieving uniform temperatures can be difficult. In order to improve the temperature field, feedback controllers have been proposed for use in hyperthermia (Babbs et al. 1986, Knudsen and Heinzl 1986, Knudsen and Overgaard 1986, Nikawa et al. 1986) and several for use in SFUS (Johnson et al. 1990, Lin 1990, Lin et al. 1990, Roemer et al. 1986).

1.3 THE NEED FOR PAIN CONTROL IN SFUS TREATMENTS

During a SFUS treatment a patient can experience sharp pain when the ultrasound strikes a bone or a nerve. Bone pain is caused by excessively hot temperatures due to the high ultrasound absorption coefficient of bone (Hynynen and DeYoung 1988). Nerve pain is due to the temperature rise of the nerve caused by the surrounding elevated temperature field or by direct ultrasonic heating of the nerve (Lele 1963). In past treatments with SFUS, when sharp pain occurred the operator had to rely on the patient's

verbal description of the pain's location. This can be inaccurate due to the patient's difficulty in locational pain judgment. In response to the patient's pain, the operator was required to lower the overall ultrasound power to alleviate the pain or to move the scan away from the area. (The same is true for other methods of heating.) However, this is counterproductive to the therapeutic goal of the treatment - to reach and maintain a target temperature throughout the treatment volume. Moving the scan or lowering the overall power can also cause a portion of the tumor to be missed or under-heated.

Since pain can be caused by the ultrasound striking bones or nerves, it would be best to avoid doing so. In order to selectively heat the tumorous areas, a comprehensive model of the site to be treated is required. However, such a complete picture of the treatment site and the area surrounding it are not always possible regardless of the imaging technique that is used. Even if a complete picture can be compiled, the current state of technology does not always allow for optimal power deposition (Roemer 1991) to avoid inflicting pain. Given that most hyperthermia treatments will treat to a patient's tolerance for pain (regardless of the method of heating) it is not surprising to learn from a successful SFUS clinical trial, that in 169 of 225 (75%) treatments studied, the temperatures achieved were limited by a patient's tolerance to pain due to excessive temperatures (Harari et al. 1991). This limitation has also appeared in many other studies. Connor et al. 1977 stated that ultrasound near bone is a major problem that needs addressing. In another study (Corry et al. 1982) it is noted that "... the most significant and limiting toxicity (to continuing a treatment) was pain associated with ..(bone)". That study also recognized that a major barrier to the advancement of

ultrasound for hyperthermia is patient pain. Out of the 31 patients that entered that study, 40% experienced pain with half of those experiencing "treatment limiting pain". All of the patients whose treatments were limited by pain were treated near sites containing bone or nerves. This limitation often manifests itself in one or two local areas of the patient requiring the overall power to be lowered throughout the treatment volume with a system that lacks flexible power deposition. Conversely, a cool spot could not always be given more power without causing excessive heating in a different area of the scan. Excessive heating has been pointed out to lead to "intolerable pain" in the clinical trials conducted by Corry et al. 1982. These limitations detract from both the uniformity of the temperatures and the percentage of temperature probes above the target. In addition, the operator was required to continually monitor temperatures and adjust the power delivered to respond to a variety of disturbances, including physiological changes and patient pain, in order to try and achieve the best temperature profile possible. Therefore, patient feedback could improve the patient's comfort and the effectiveness of the treatment.

1.4 UNDERSTANDING PAIN

The goal of a hyperthermia treatment is to achieve the best possible heating of the target volume without inflicting intolerable pain to the patient. Since the operator of a SFUS treatment often treats to the patient's tolerance for pain, this presents the operator with several problems which include: how to identify the pain, the determination of

important factors in pain sensation, and when does pain become excessive? In order to answer these questions it is necessary to look at the mechanisms behind pain.

1.4.1 WHY WE FEEL PAIN

The word pain has its origins in the Greek word for penalty (Webster 1981) which indicates that pain is an unwanted consequence of ones actions. This leads to one of the main reasons that pain exists in nature, to alert the body of impending damage. The sensation of pain can be traced back in evolution over the last 250 million years where the first modern pain receptors have been found in mammals of that era (Miller 1967). The reasons behind evolution's drive to develop such complex mechanisms as pain sensations can be seen if one realizes that the sensation of pain is the motivational force to drive organisms into action aimed at stopping the pain as soon as possible (Miller 1967) and thus prolong survival. A detailed account of the biological mechanisms of pain in man can be found in Kiff 1974 and many other sources, therefore pain sensation will only be briefly summarized here.

1.4.2 HOW PAIN IS SENSED

Pain sensation is vastly different between skin stimulation and deep structure stimulation. The skin is the body's first line of defense against damage and thus has the ability to accurately localize and categorize pain. An animal would develop accurate

skin sensation because it has provided a survival advantage to the species in the past (Moran 1950) by alerting the animal before the source of the pain inflicts a debilitating or mortal wound. This is in contrast to pain felt deep within the body which is commonly sensed away from the source of the pain (Moran 1950, Iggo 1972). For example, a heart attack victim commonly feels pain in the arm instead of the heart. While the phenomenon of pain referral is not completely understood it is speculated that it is a case of "faulty localization" by the brain (Moran 1950). Accurate pain sensation deep within the body has never evolved because there has never been an evolutionary reason to do so (Moran 1950). The only deep pain information that is useful to the survival of an organism is the existence of the pain.

When a painful stimulus is applied to the body, a threshold level must first be exceeded which causes the firing of nerve impulses. Once activated, it is then possible to see a double response to the pain (Livingston 1943). The first response is the "fast response" which is transmitted by heavily myelinated nerve fibers at speeds up to 45 meters per second- carrying the pain information to the brain from as far as the foot in as little as 0.1 second (Iggo 1972). Up to one full second can pass before the brain receives the "slow response" which is carried via nonmyelinated fibers at speeds around 1 meter per second (Iggo 1972). The slow response gives the brain the important detailed information about the pain's location and type of stimulus that the fast response lacked. The parts of the brain that are involved with the pain sensation include most of the major higher brain centers. The higher brain centers can affect the lower level reflex response (Miller 1967). For example, if one was to pick up an extremely hot cup of tea in an

expensive cup, the hand will still jerk away but not drop the cup. This demonstrates that after the brain perceives pain it must process the pain information on several levels and then select the appropriate response and act upon it. Since the modifications made to the SFUS system require the patient to press a button in response to pain (presented later) the above reaction times should be kept in mind.

1.4.3 PAIN, THERMAL STIMULATION, AND DRUGS

Several studies have been carried out to determine the relationships between power deposition, tissue temperature, and pain sensation (Hardy 1953; Hardy and Stolwijk 1966; Hardy et al. 1967). From experimentation done on artificially blackened spots on the human forehead and on the back of human hands, it is possible to find approximations relating tissue temperature and the amount of steady state power required to reach the pain threshold. The experimental setup that Hardy used consisted of an intensity controlled radiant heat source that was separated from the subjects being tested by a shutter. This system exposed the subjects to a step increase in radiant heat exposure when the shutter was opened. The resulting temperature rise at the skin of the subject would then approximate an exponential function of time and the radiant intensity. These studies found that the sensation of pain depends solely on the elevation in the temperature of the tissue as long as the intensity of the radiation was sufficient to elevate the skin to a painful temperature. This is in contrast to tissue injury which was found to depend on both the temperature and the duration of heating (Hardy et al. 1953). The dependance

of the sensation of pain on the skin temperature can be seen by looking at equation 1 which was found by Buettner and used by Hardy after exposing 6 subjects to different levels of radiant heat and measuring the corresponding time to reach the pain threshold in 90 different experiments.

$$T_s = T_0 + Qk\sqrt{t} \qquad (1)$$

Where T_s = skin temperature at the pain threshold (°C); T_0 = initial skin temperature before irradiation (°C); Q = intensity of radiation (mcal/sec/cm²); k = an experimentally determined constant = 0.032; and t = time of exposure in seconds.

When Hardy used equation 1 to calculate the skin temperature at which the a given intensity evoked a pain response, he found that a temperature of 45.7 °C with a standard deviation of 1.7 resulted from all experiments regardless of the length of time or level of power used which agreed closely with experimentally gathered temperatures. Since higher intensities of radiation will cause a faster temperature rise on the skin being exposed, the time rate of change of temperature at the skin surface (dT/dt) is a major factor in the amount of time that is required for the pain threshold to be reached at a given temperature; i.e., a fast temperature elevation (from a high intensity of stimulation) will result in the pain threshold being reached sooner. The temperature of 45.7 $\pm$ 1.7 °C puts limits on the applicability of equation 1 because a skin temperature of 42 °C would be out of this range and would therefore not cause pain. However, there is variance in the pain threshold (T_s) over different parts of the body. The heel of the foot has the highest threshold, and the lower back, buttocks and thighs have the lowest

threshold to a painful stimulus (Hardy et al. 1967). The pain threshold will also be lower in areas where the tissue has been previously damaged. Rapid repetition of stimulation to the same area will also lower the pain threshold by causing sensitivity to the stimulus until habituation occurs- after which time the threshold will increase (Hardy et al. 1967). A pre-existing pain in one area can also cause an increase in the pain threshold in a different area of the body (Hardy et al. 1967). (This is the rationale behind the practice of "biting the bullet" during painful procedures such as tooth extraction without the benefit of anesthesia.) This could be caused by an overload of the nervous system or the body's production of natural pain suppressors created by the first pain sensation. The pain threshold can also be increased by a person's attitude, with one study reporting that 20% of subjects tested experienced an increase in the pain threshold by repeating the phrase "I don't feel the pain" (Hardy et al. 1967). The same study also found that 90% of subjects tested reported an increase in the pain threshold when placebos were administered (Hardy et al. 1967). Overall, 30% of all patients in pain can expect pain reduction from the administration of medically inert substances (Kiff 1974).

More powerful than placebos are analgesics. A drug is classified as an analgesic if it is able to act on the nervous system in such a way as to reduce or eliminate pain without producing unconsciousness (Hardy et al. 1967). Analgesics work principally by blocking the action of peptides which are formed in the extracellular fluid whenever tissue damage occurs (Kiff 1974). There are numerous factors that must be considered in the evaluation of analgesics. Some of the important factors are given by (Hardy 1967 et al.) as:

"1. The pain threshold-raising effect;
2. The pain reducing effect;
3. Reducing of pain by suppression of visceral and somatic effects themselves pain inducing;
4. Alteration of attitude toward pain by promoting feelings of well-being and freedom from anxiety on the one hand. or depression or excitement on the other;
5. Sedative action, inducing sleep;
6. Side effects involving nausea, vomiting, and constipation;
7. Toxic action, particularly suppression of respiration, and allergic reactions;
8. Total effect upon the patient, involving questions of whether the patient "feels better", and whether the analgesic is suited to administration in the particular patient."

CHAPTER 2.0: SYSTEM DESCRIPTION

2.1 EXISTING SYSTEM BEFORE MODIFICATION

The system used to implement this study began as a commercial diagnostic ultrasound unit (Octason by Ausonics Pty. Ltd., Sydney, Australia) that was modified to produce hyperthermia for the treatment of cancer (Hynynen et al. 1987). To induce elevated temperatures. six high power 1 MHz focussed ultrasound transducers have been mounted onto the imaging gantry. The focus of each transducer is aimed at a common

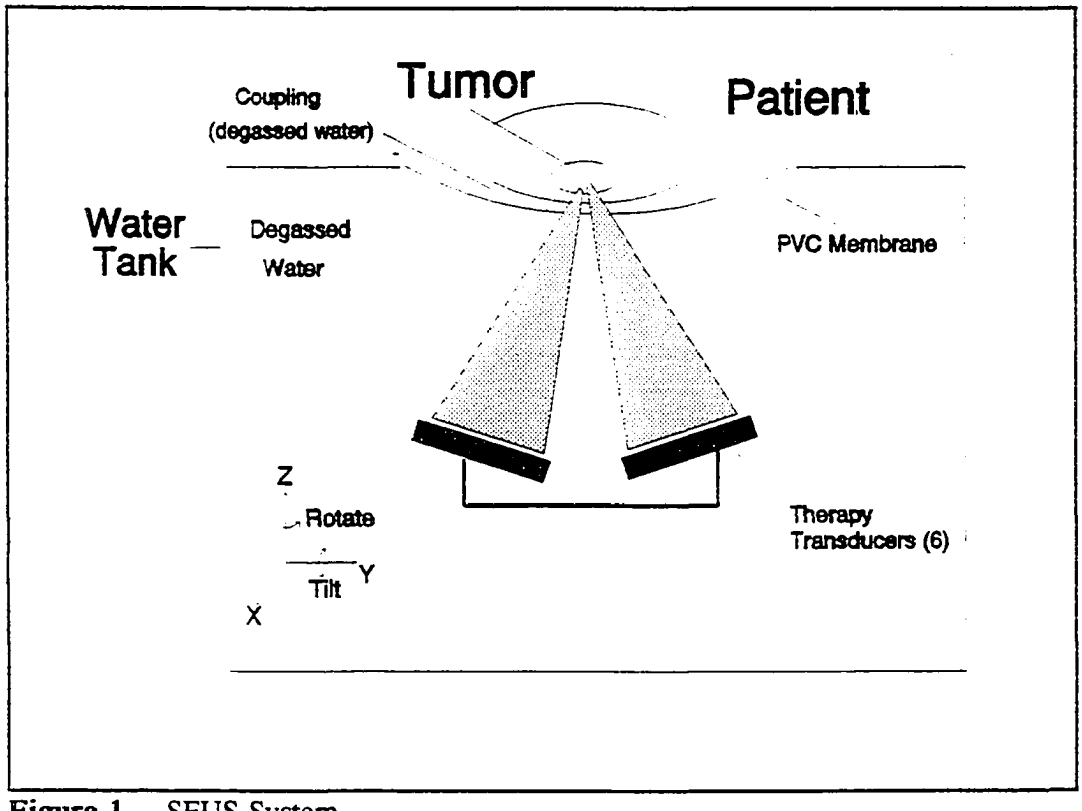

Figure 1. SFUS System.

point (Figure 1). The gantry possesses five degrees of freedom (X, Y, Z, rotate, and tilt) but only two dimensional concentric X-Y octagonal scans were used. Gantry motion is controlled by an Apple IIe computer (Cupertino, CA) and programmable stepper motor indexers (Anaheim Automation, Anaheim, CA). Positional feedback potentiometers installed on the gantry provide the Apple with a locational safety check. The RF voltage for driving the amplifiers is generated by a frequency generator (Wavetek model 271, San Diego, CA) and then amplified by a six channel power amplifier (URI Thermics). The temperatures were monitored using seven sensor manganin-constantan thermocouple probes. The thermocouple voltages were measured sequentially by a digital voltmeter (HP 3456A) via a data acquisition system (HP 3497A) and converted to temperature by the HP computer (HP 9836). Figure 2 shows a system block diagram for the hyperthermia equipment before modification for this work.

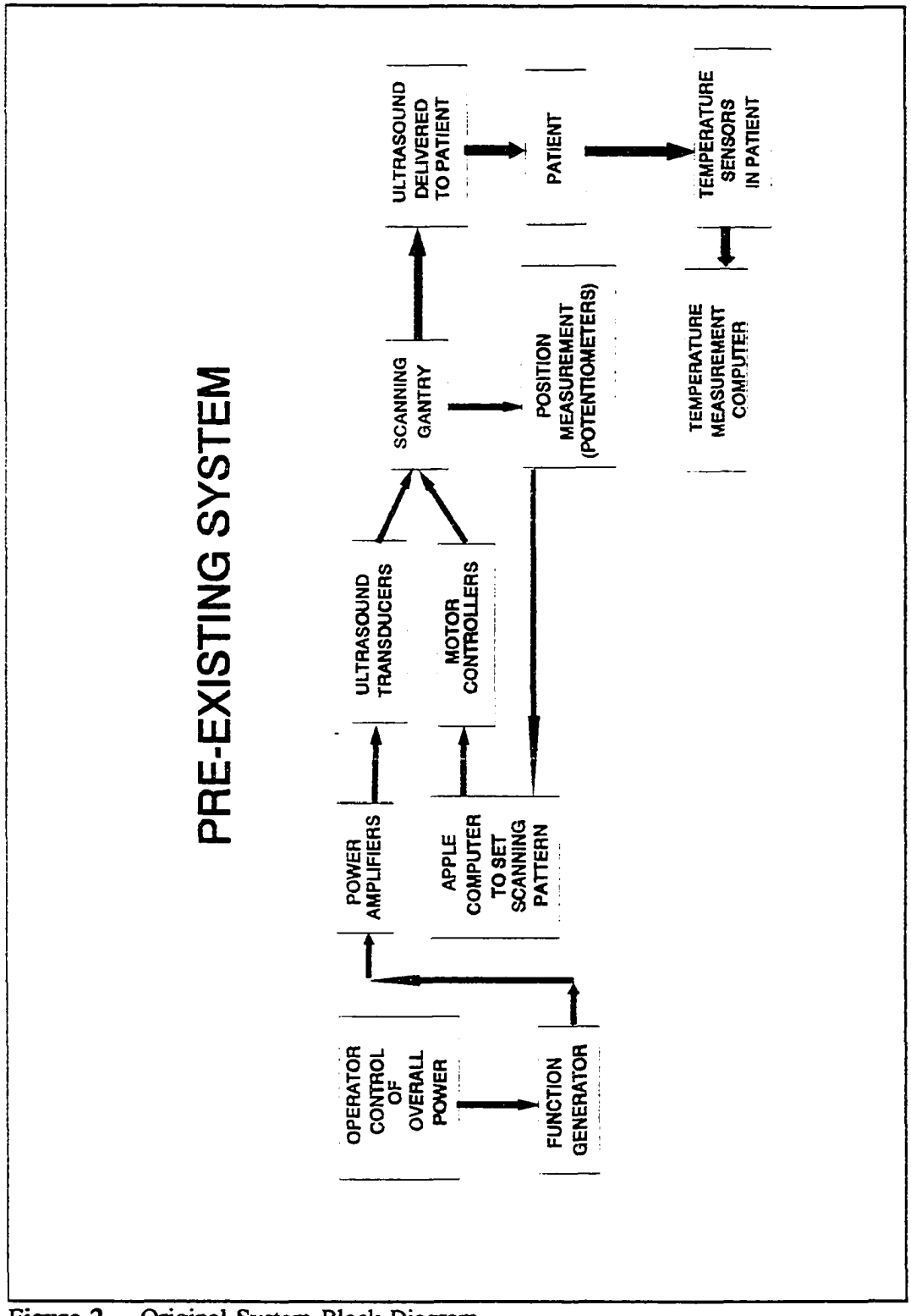

Figure 2. Original System Block Diagram.

2.2 LIMITATIONS IN THE EXISTING SYSTEM

The SFUS system at the University of Arizona did not originally have any practical means of controlling the ultrasound power as a function of scan position during patient treatments. The power field could be increased or decreased as a whole, and the power of each transducer could be varied as well as the frequency of the transducers. In addition, if a patient experienced pain during a treatment, the entire scan would have to be moved away from the area of discomfort or the overall power would have to be lowered in order to relieve the discomfort. This work was undertaken with two basic goals in mind. First, to provide the operator with a robust temperature feedback controller to modulate the ultrasound power as a function of scan position in order to improve the temperature field. Second, to obtain direct feedback from the patient as to when pain is experienced and use this information to alter treatment parameters in order to alleviate the pain.

2.3 NEW SYSTEM DISPLAY

To improve the above mentioned limitations in the University of Arizona SFUS system many additions and modifications have been made to the system described in Section 2.1. One of the first additions to the system was a treatment display screen.

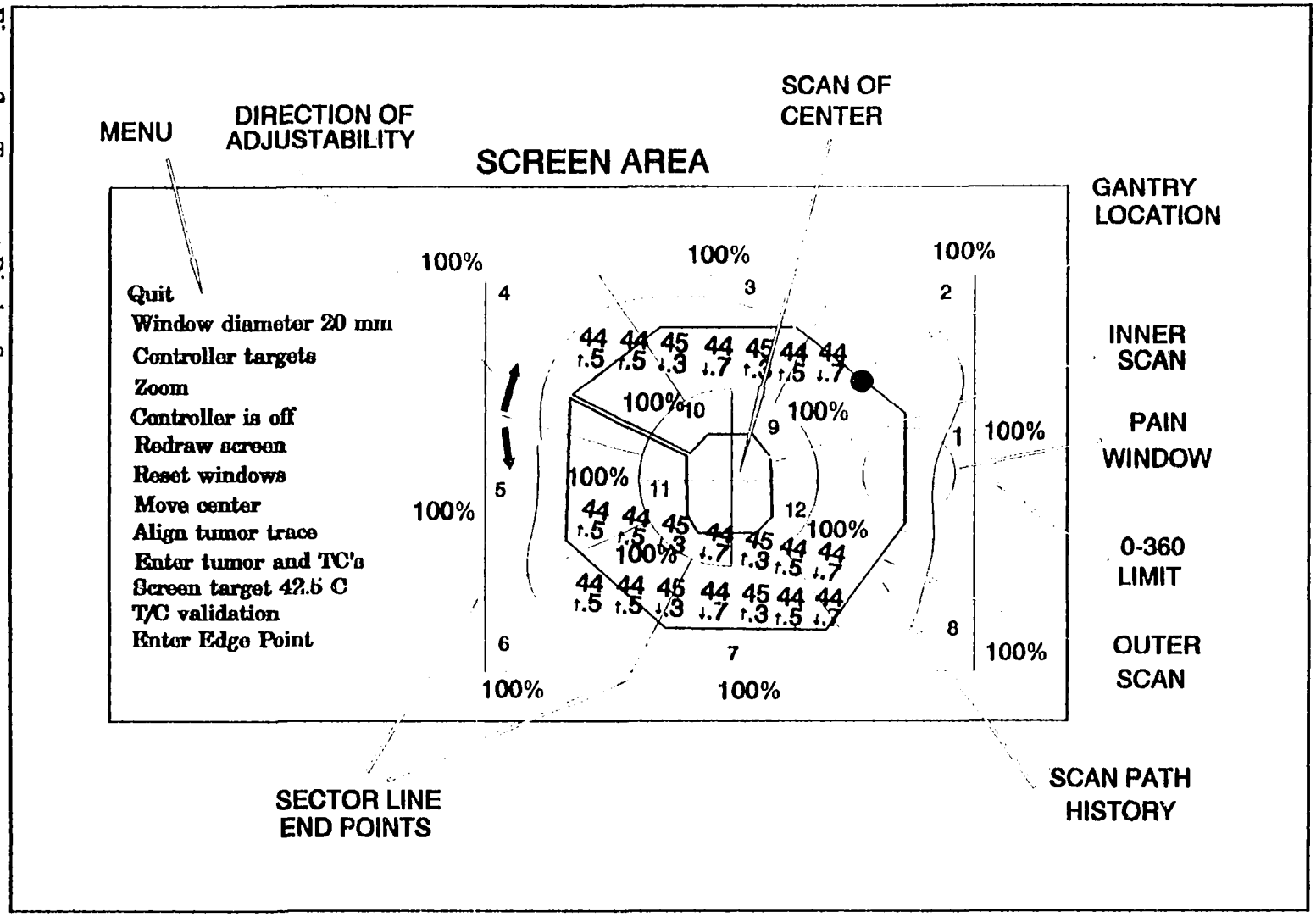

Figure 3. Treatment Display Screen.

Figure 3 shows the display screen during a typical treatment. The actual screen has the benefit of color to distinguish the different elements of the screen from one another. There are two main parts to Figure 3, the menu to the left and the graphic display area to the right. Both parts of the display are described below.

The menu lists the different commands that are available to the system operator during a treatment. A moveable check mark (not shown) to the left of each item in the menu list is used to indicate which menu item is to be selected. The meanings and restrictions on the use of the commands is described in detail in the users manual located in Appendix A.

The following procedure is used to enable the temperatures to be displayed in their correct locations and to allow the controller to assign thermocouples to the proper sectors: first, before the start of a treatment a transparency is placed directly on the patient over the site to be treated. Next, a rough tumor outline is marked, and the insertion sites of the temperature probes are marked along the axis of the insertions. This information is combined with length calibration marks on the probes to determine the depth of penetration. This information is then drawn on the transparency. An alignment mark is then made on the patient and on the transparency which indicates the center of the scan. The information on the transparency is then entered into the Vectra computer using the graphics tablet.

The lines of numbers in the graphical portion of Figure 3 represent thermocouple temperatures displayed with the decimal point indicating the thermocouple's position relative to the rest of the scan parameters. Each temperature probe has seven

thermocouples arranged in a line as shown in Figure 3. The color of each temperature displayed will be blue if the temperature is below the screen target (set by the operator and described in Appendix A 3.11) and it will be red if above. Above the decimal point, a small arrow will appear if the current temperature for each thermocouple is different than the previous temperature for that thermocouple by more than 0.1 °C. The arrow will be red and point up if the current temperature is hotter than before or blue and point down if it is colder. The temperature colors and arrows are only for display and have no other effect on program execution. If a temperature is less than 0 °C or more than 80 °C, it is assumed to be an invalid temperature reading and only the decimal point is displayed.

The small solid circle in Figure 3 represents the gantry position. On the actual screen it is represented as a brilliant yellow ball (know as "Scott's Comet") that leaves a trail to mark its previous positions. The trail will be white if the gantry is currently in an outer scan and it will be green during an inner scan. The trail of past gantry positions will accumulate until the screen is redrawn by moving a sector line or one of the following menu commands: REDRAW SCREEN, ZOOM, MOVE CENTER, or ALIGN TUMOR TRACE AND TC'S all of which are described in Appendix A. The buildup of the trail allows the gantry scan path history to be viewed, and allows any gantry drift to be readily visible. Occasionally, the trail of past gantry positions may become noisy creating a haze around the scan path. This is due to noise on the electrical lines of the hospital or from interference from the ultrasound transducers on the position signals. The noise will have no adverse effects on the treatment as long as the magnitude of the noise

does not become excessive in comparison to the size of the scan. A first order low pass filter has been installed on the signal lines to help alleviate as much of the noise as possible.

The radial lines in Figure 3 are used to show how the scan field is divided into eight radially adjustable sectors and four inner radial sectors for a total of twelve temperature control regions. The boundary between the inner and outer scan regions used by the power control (described later) is shown in Figure 3 as a circle that is concentric with the center of the scan. The solid arrows in Figure 3 were added to illustrate the direction of adjustability for the radial sectors.

2.4 COMPUTER CONTROL OF TEMPERATURE

Computer control of ultrasound power as a function of scan position would result in a significant improvement in SFUS treatments. Two methods of control are provided. The first method is manual control of power for each of the 12 sectors in Figure 3 and the second method uses a temperature feedback system.

2.4.1 MANUAL POWER CONTROL

If the cursor keys are used to move the menu pointer past the top or bottom of the menu list (described above), the pointer will move to the perimeter of the gantry display screen. If the menu pointer is advanced all the way around the perimeter and there is an

inner scan, the menu pointer will then advance to the perimeter of the inner scan around it, and then back to the menu list. When on the perimeter, the menu pointer will alternate between a power adjustment for that sector (represented as 100% in Figure 3) and a sector line end point. Sector lines are used by the program to define independent areas for power control as a function of gantry position. Whenever the gantry enters a new sector the ultrasound power will be adjusted to the percentage specified for that sector (either by manual control or the automatic temperature controller). The power adjustment can be in two forms depending on the state of the temperature controller. A percentage of between 0% and 100% with adjustable increments of 10% will be shown if the temperature controller is OFF (as seen in Figure 3); or, the controller target temperature will be shown for that particular sector in degrees celsius with adjustable increments of 0.1° C if the temperature controller is ON (the 100% shown in Figure 3 would be replaced by the target temperatures). The "+" and "-" keys on the right of the keyboard can then be used to either move the sector lines radially cw or ccw in 5 degree increments or to adjust the power or target temperature up or down as described above depending on which one (sector line end point or power/target temperature adjustment) the menu pointer is on when the keys are pressed. The program puts two restrictions on sector line movement: the first is that one sector line cannot cross over another line, and the second is that the first and last sector lines cannot cross over the 0-360 degree line which the pain program defines as residing at the middle right portion of the screen.

2.4.2 TEMPERATURE FEEDBACK SYSTEM.

This section will describe how the uniformity of the temperature field in the tumor is improved while relieving some of the operator's responsibilities in temperature monitoring and power adjustment by use of a modified implementation of the controller described by Lin et al. 1990, Lin 1990.

The software developed for this section is essentially two dimensional as is the present scanning pattern utilized by the SFUS system. The patients however are not two dimensional but a sub-class of their tumors can be considered as being two dimensional; such as breast tumors. Breast tumors and the surrounding areas are of somewhat uniform thickness and require temperature probes to be placed parallel to the plane of the scan.

The assumption was made that during a successful treatment limited thermal coupling would generally exist between the sectors that were shown in Figure 3. That is, when the temperature field is close to being uniform, the thermal conduction between adjacent regions is small and can therefore be neglected. If the controller works well this assumption would still be valid even under conditions of highly nonuniform blood flow because a good controller would control the power in such a way as to improve the temperature field until the effects of thermal coupling are small and can be neglected. The assumption of limited thermal coupling then allowed each sector to be given an independent modified version of the single input single output (SISO) bang-bang/PID

controller developed and analyzed by Lin et al. 1990, Lin 1990. A block diagram of this controller can be seen in Figure 4.

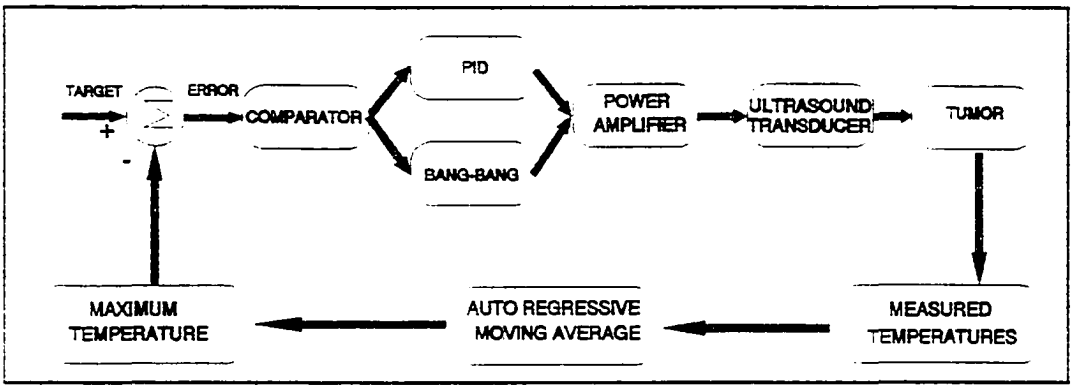

Figure 4. Controller Block Diagram.

The analog form of the controller is given in equation 2.

$$P = \begin{cases} P_{max} & if\ T_{target} \le T_1 \\ K_p\left[e(t) + \frac{1}{\tau_i}\int_{t_i} e(t)\,dt + \tau_d \frac{de(t)}{dt}\right] \le P_{max} & if\ T_1 < T_{target} < T_2 \\ 0 & if\ T_2 \le T_{target} \end{cases} \quad (2)$$

Where T_{target} = target temperature; T_1 and T_2 are the upper and lower limits for the bang-bang controller such that when the measured temperature is between T_1 and T_2 the PID portion of the controller is used; P_{max} = upper limit for the amount of power that can be delivered (zero is the lower limit for power that can be delivered); P = power selected by the controller; e(t) = difference between the measured and target temperatures; K_p,

τ_i, and τ_d, are the proportional gain, integral or reset time, and derivative time, respectively.

The PID section of the controller is written in digital form by using a backward difference approximation for the derivative, a trapezoidal numerical integration for the integral, a sampling time of 30 seconds, and a gain of 0.4 (Lin et al. 1990, Lin 1990) (equation 3).

$$P_n = \begin{cases} P_{max} \\ \dfrac{44e_n - 4e_{n-1} + 15\sum_0^n e_j}{100} \\ 0 \end{cases} \qquad (3)$$

In equation 3, n = the current time step; n-1 = the previous time step; P_n = power at time step n; e_n = difference between the measured and target temperatures at time step n; $\Sigma_0^n e_j$ = the sum of all the errors from n = 0 to the current time step.

The main features of this control law are that it gives fast rise times when the temperatures are low, fast drop off times when the temperatures are high, and an accurate PID controller when the error is small (Lin et al. 1990, Lin 1990). To reduce the effects of noise and seasoning, an auto regressive moving average (ARMA) was employed to express the controller input temperature in terms of a linear combination of

the current and previous measured temperatures. The weighting factors for each of the temperatures in the temperature history were experimentally determined (by Lin et al. 1990, Lin 1990) for use on the same system as the one used for this study. Equation 4 shows the relation used.

$$T_c = 0.35T_n + 0.3T_{n-1} + 0.2T_{n-2} + 0.15T_{n-3} \quad (4)$$

One property of a controller that contains an integrator is that it will try to drive the integrand (which is the error signal) to zero. This can be a potential problem when the error stays either above or below the saturation level of the input for an extended period of time (integrator windup), thus accumulating a large area under the error curve. Then, if the error switches to the other side of the saturation level, the controller would need to counteract the large area accumulated by the integrator previously. This leads to large overshoot and errors (Franklin et al. 1991, Middleton and Goodwin 1990). Integrator windup is avoided by integrating the error (or summing the error when using discrete time) only when the error is between the bounds of the bang-bang portion of the controller (between T_1 and T_2), thus reducing the area under the error curve yielding and a faster response time. The anti-integrator windup is utilized throughout a treatment whenever the error for a sector is outside of the bounds of the PID section ($T_{current} > T_2$ or $T_{current} < T_1$).

One drawback of using a SISO controller analogous to Lin's is that it required preselected thermocouples to be used as input for each sector that was to be controlled. In order to let the computer select the input to the controller for each region in real time, and to accommodate multiple thermocouples in each region, the thermocouple in each sector with the highest temperature according to equation 4 (ARMA) is used for the input to the controller for that sector. The maximum is selected in order to prevent run away temperatures and to help prevent the controller from saturation caused by trying to raise the temperature of a control thermocouple that was not significantly affected by the applied power.

A potential problem with a PID controller can occur during the transition from manual to computer control if the error is close to zero. The controller would begin operation with a small error, and since this would be the first time through the control law, the integral of the error would also be small. This condition would yield a low power setting. If the power was at a high level to achieve the previous temperatures, the resulting low power setting from the control law would produce a dip (or bump) in the temperatures. The problem is more severe if the control temperature is above the target temperature but still requires attention when the control temperature is below the target temperature. In order to achieve a bumpless transition to automatic control (see Astrom

and Wittenmark 1984 or Middleton and Goodwin 1990), the sum of the error term in equation 3 was initialized according to equation 5 which was derived from the PID section of formula 3 by setting n = 0 and solving for the summation term.

$$\sum_{-\infty}^{0} e_j = \frac{200P_0 + 8e_{-1} - 88e_0}{30} \qquad (5)$$

Equation 5 would give the same power level after transition to the control law as was required before transition, thus creating the bumpless transfer.

2.4.3 SOFTWARE STRUCTURE

The program to implement this work was written in Microsoft Basic version 6.0. Microsoft Basic offered the advantage of being able to create code that could be compiled and run more quickly while still maintaining a somewhat universal understanding among fellow programmers. The source code contains comments detailing the function of each line. The variable declarations contain comments that explain the purpose, meaning, or range of acceptable values for all variables used in the program.

2.4.4 PROGRAM LOOP

The program written to implement this work is structured with three levels of code. These levels of code can be categorized into the program loop, main program, and the error handler. Before the program enters the program loop (Figure 5), all of the variables are initialized, the data array are declared, and all of the communication lines with the I/O cards, graphics tablet are configured, and the patient data files are opened. The program loop was written so that it is possible to acquire user keyboard input while still executing the main program. This was done by first calling the main program and then checking to see if there has been any keyboard input. If keyboard input occurs, the keyboard interrupter section is called. The interrupter section was written in a manner to avoid requiring the computer to wait with statements like INPUT, which demand 100% of the computers

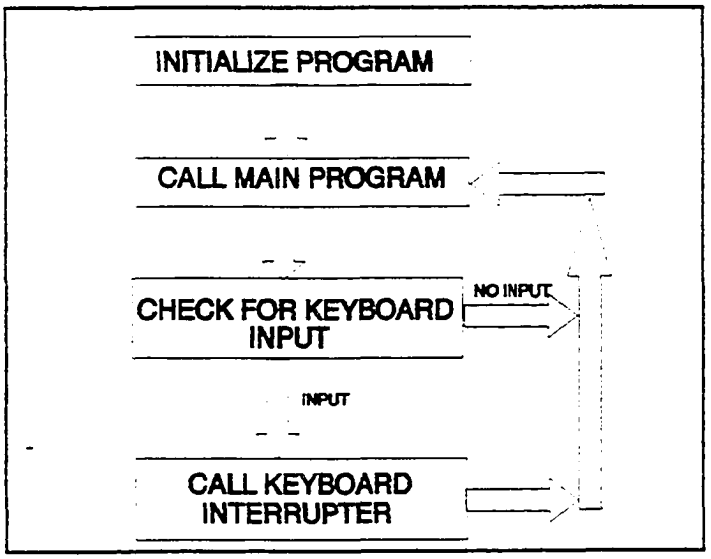

Figure 5. Program Loop.

attention until input is received. By using the INKEY$ command, which checks the keyboard and then continues, it became possible to write keyboard data entry code that would both interrupt key presses and call the main program without any noticeable delay to the user.

2.4.5 MAIN PROGRAM

The main program contains the temperature controller, pain button algorithm (described later), all data input and output, and screen graphics routines. The entire section is structured so that when called, there are no delays or loops in the code. This allows the program loop to operate as quickly as possible. The methods used also streamline program execution by allowing this section to be called at a faster rate increasing the data I/O sample rate. Streamlining was accomplished by an extensive application of data flags to keep track of the current state of all major operations. To further enhance the optimization of this section, decision blocks are used to skip potentially time-consuming operations like data I/O when they are not needed. A complete block diagram of this section can be seen in Figure 9.

The main program also acquires and displays temperature information over the IEEE bus. Since the Vectra computer is configured as a peripheral on the bus it is therefore required to wait for data to come across the bus; verses commanding that it be sent. There are two basic methods for detecting when data is being sent. The first would have the program continuously check the state of the bus for data. This method is

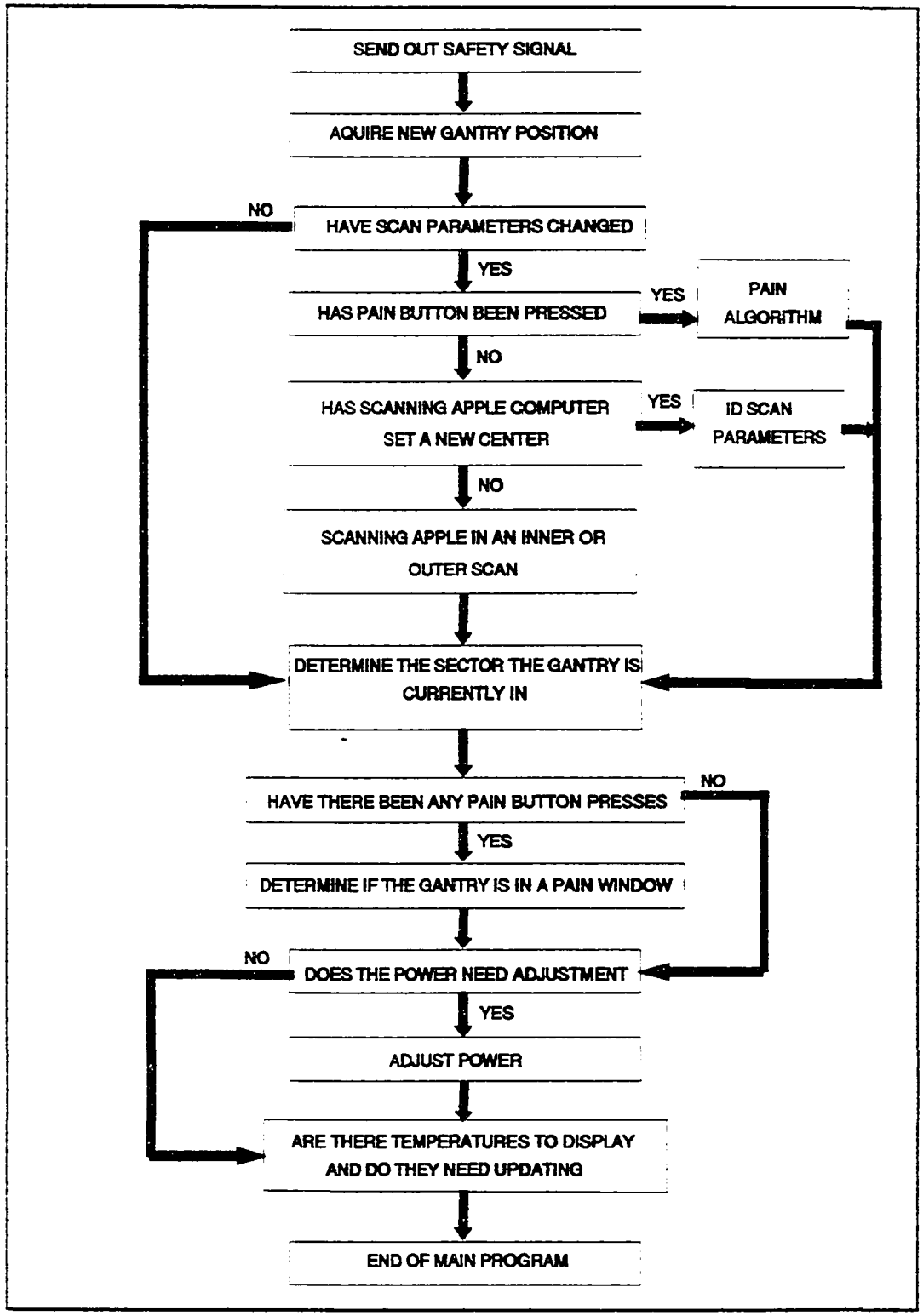

Figure 6. Main Program Block Diagram.

extremely slow, taking up to one microsecond per check, which would effectively cut the program data sample rate in half. The other method would set up a program interrupt to cause the program to jump to a 'read data bus' routine whenever data is present. Since the later is done at a machine code level it is far faster and does not use as much valuable CPU time when not needed. Because of the speed advantage, the interrupt method is used. (It should be noted that this interrupt can be rendered inoperable by an incorrect installation of device drivers in the CONFIG.SYS boot file of the Vectra computer. Device drivers for components like a mouse MUST be installed before the device driver for the A-488 card.) Data is sent over the bus two temperature probes at a time. Each set of probe data is stored in a data array until the count on the number of probe data sent matches the number that the pain program is expecting at which time a flag is set to cause the main program to update the temperature display and call the temperature controller (if it is activated).

2.4.6 ERROR TRAP

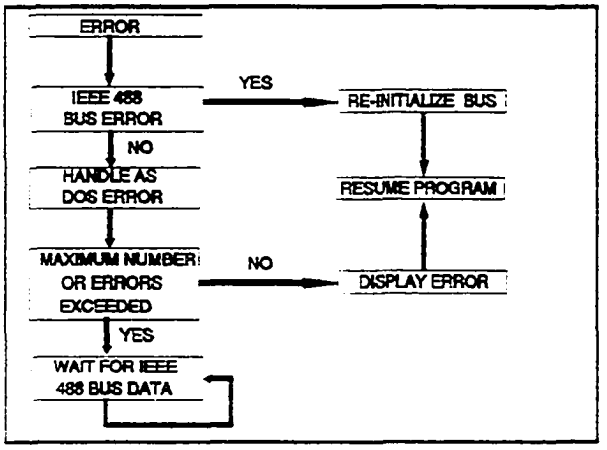

Figure 7. Error Handler Block Diagram.

Since a program crash would have adverse effects on both the effectiveness and more importantly, the patient's safety, an error handler becomes a necessity. During the execution of an application specific program over 4000 lines long, there are many types of errors which can occur which do not warrant shutting down the entire treatment system. Examples of non- treatment threatening errors would include trying to locate graphics outside of the acceptable range, a bad reading from one of the I/O cards, invalid user input, or a program operator using the program in situations that have not yet been conceived. While the first three above mentioned errors have been accounted for, accounting for the third is not possible. The error handler outlined below tries to separate critical errors from non-critical ones.

The error handler (Figure 7) for the program is initialized by setting a program interrupt to jump to a special section of code to deal with an error when it occurs. Without the interrupt the program would stop execution when an error is detected. The code that the program jumps to first checks for the most likely source of the error; the A-488 bus. If the bus is the source of the error, the error handler will re-initialize the bus and then resume program execution. If the error was not a bus error, it is assumed

that there may have been a pain program error. If this is the case, a counter is incremented and program execution is resumed in the hope that the error which occurred will not occur again. If the number of errors exceeds 20 (an arbitrary number) there must be a more serious flaw in the code and all program activities are halted except for the reading of the A-488 bus to prevent the HP temperature computer from hanging up and the power is set to 0%. At this point the interrupt method for reading the bus is no longer available so the first method of bus control is used.

2.4.7 HARDWARE FOR COMPUTER CONTROL OF TEMPERATURE

Several hardware additions to the system shown in Figure 2 were made for this work. These additions are shown in Figure 8. The most significant addition in Figure 8 is a HP Vectra QS/20 (Hewlett Packard,Cunnyvale, CA) 386 computer. The 386 computer was integrated into the old system by tapping into the gantry positional information generated by the position measurement potentiometers and scan information from the Apple scanning computer. The temperatures from the temperature measurement computer are sent to the Vectra QS/20 over an IEEE-488 bus between the computers. Thermocouple spatial information is entered into the 386 by the use of a digitizing graphics tablet (Summagraphics Corporation, Seymour, CT). The 386 computer can control ultrasound power by commanding a duty cycle controller box which intercepts the function generator output before the signal goes to the power amplifiers.

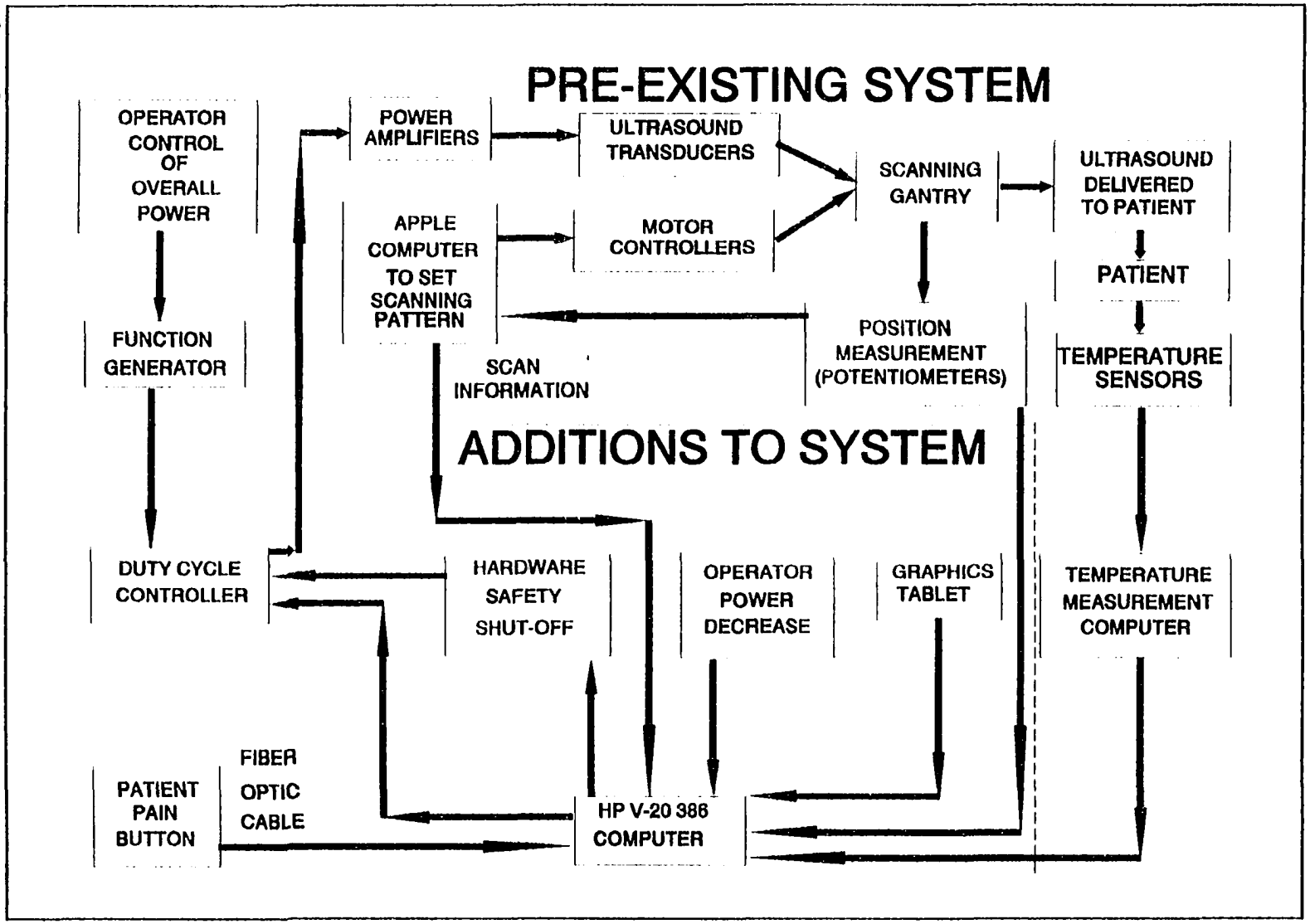

Figure 8. Modified System Block Diagram.

The duty cycle controller box has six independent channels each capable of imposing a duty cycle of between 0% and 100%. At the current stage of development, all six of the channels are controlled in unison. The duty cycle controller operates by ANDing three signals together to form the output for each channel. The first signal is formed from a 100 Hz spike trigger that was generated by a free running 555 timer (Figure 9). The trigger signal is then distributed to six 555 timers that are configured to generate one pulse for each trigger spike. The duration of the pulses from each mono shot timer is determined by analog voltages generated by the Data Translation 2811 D/A card installed in the Vectra computer. As long as the duration of the pulses are less than the length of time between the trigger signal pulses, a 100 Hz duty cycle signal is generated. Thus, if the length of the mono shot timer pulses are three quarters of the length between the trigger pulses, a 75% duty cycle is generated (Figure 9).

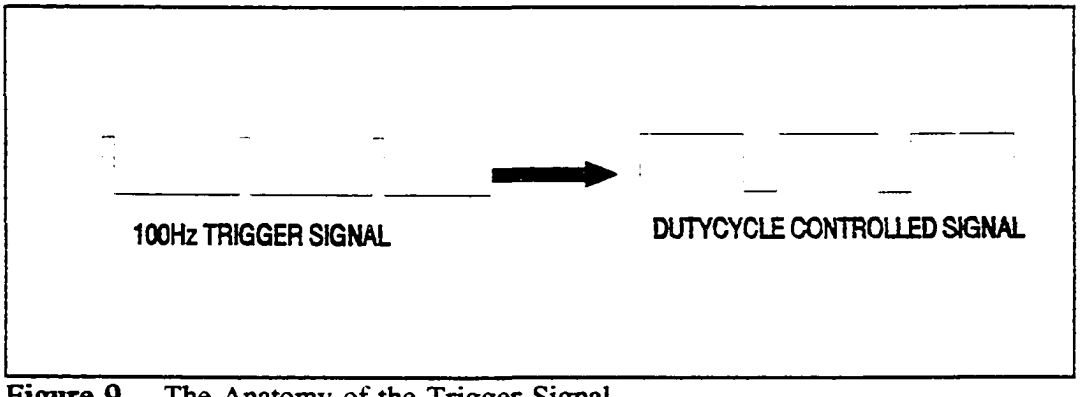

Figure 9. The Anatomy of the Trigger Signal.

The duty cycle signal is then the first signal that is fed into the AND gate (Figure 10). The second signal is the input signal to the box which must be a TTL compatible signal of any frequency greater than about 1000 HZ (Figure 10). The 1000 Hz restriction is imposed because the signal being controlled must have a frequency at least 10 times greater than the frequency of the duty cycle signal for the scheme to be effective. The hardware safety shut-off is the third signal into the AND gate. The safety signal is the output of a CD4538 timer (Figure 10) which will remain high as long as the program on the Vectra computer is running. This is accomplished by having the main program send one pulse of a square wave TTL signal that is generated by the Data translation 2801 digital I/O card. This safety signal is used to continuously trigger the CD4538 timer. Therefore, if the safety signal stops for any reason (such as a computer crash or program bug), the output of the safety timer will go low, disabling the output of the AND gates

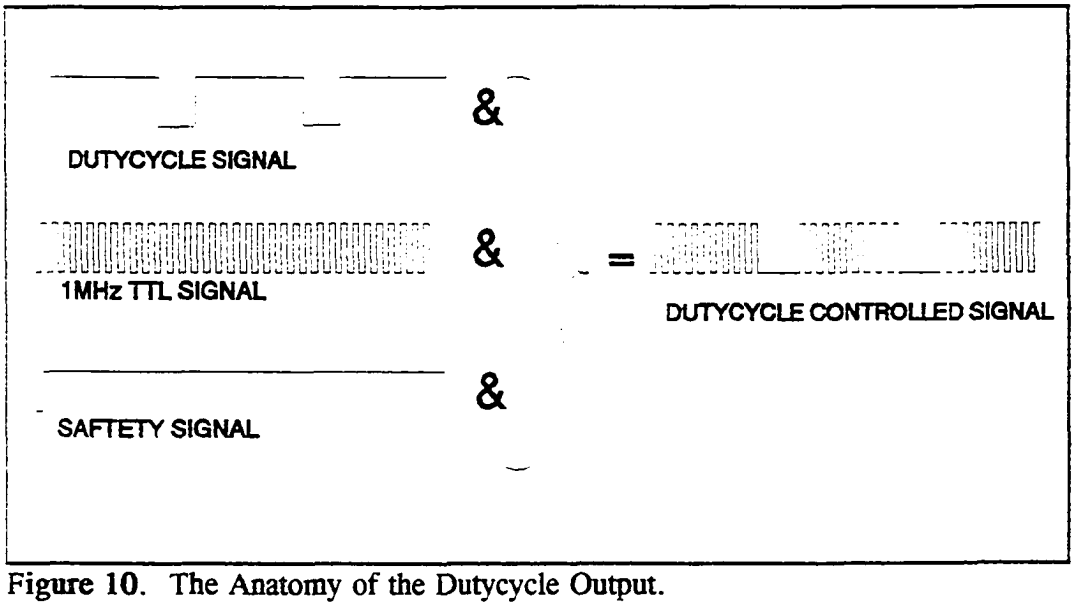

Figure 10. The Anatomy of the Dutycycle Output.

and effectively shutting off power to the transducers. Appendix C shows a complete schematic for the duty cycle box.

2.5 INTERACTIVE PAIN BUTTON DESCRIPTION

In order to identify the area of patient discomfort, an optically isolated button was constructed which is referred to as "the pain button" (Anhalt 1991). When in the hand of a patient, the pain button allows the program monitoring it to get direct input from the patient as to the approximate location of any pain. This bypasses the slow and inaccurate verbal identification procedure that existed previously. The pain button is most effective if the pain appears and disappears quickly in the same location with the same period as the repetition of the gantry scanning pattern. This type of cyclical pain can occur when ultrasound strikes a bone or a nerve and will usually be sharp pain in nature. It is this type of pain that the focus of this portion of this work.

In order to correlate the position of the gantry at the time of the pain the patient is asked to press a pain button that is monitored by the Vectra computer. Throughout the rest of the treatment, the program adjusts the duty cycle (power) of the ultrasound whenever the gantry location is close to a stored pain button press location.

2.5.1 PAIN BUTTON ALGORITHM

The goal of the following algorithm is to alleviate the pain while administering as much power to the patient as possible. During the development of this algorithm any decisions or assumptions that had to be made were done in such a way that any potential errors would be on the side of patient safety, in contrast to being on the side of best temperatures or most ultrasound power delivered. To this end, most button presses lower the power. A method was required to deal with multiple pain locations and to account for the fact that the location of the gantry at the time of the press will move past the pain's true location due to a patient's finite reaction time. Patient reaction time is an uncertain quantity due to medications, slow reflexes, or poor physical/mental patient condition as discussed previously.

The algorithm works by searching for the correct delay time of the patients reactions to pain and by finding the correct size and location of the area that is causing the pain. The program then lowers the applied power in that area to a level that is as therapeutic as possible while not being intolerably painful. This algorithm is described herein for one pain location and thus one series of windows. However, the program can apply the algorithm to multiple locations simultaneously. The limit on the total number of windows at any one time is 200 (the previous version of the program had a limit of 300 pain button presses throughout the entire treatment). If the limit is exceeded, the program will beep repetitively and display a message stating that no more presses will be accepted.

All displayed window powers (and all powers discussed below) are a percentage of the maximum absolute power of the sector that they are in. For example, if a window with a power setting of 50% is in a sector with 80% power, the absolute power would be 40% of the maximum power. If a window area overlaps two sectors of different power levels, the absolute power when the gantry position is inside the window will change accordingly when the gantry crossed the sector boundary (Figure 11).

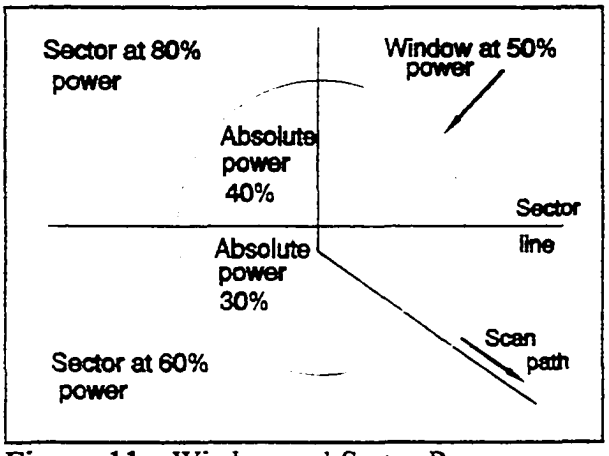

Figure 11. Window and Sector Power.

The pain button algorithm was limited to three windows in any one series based on the basic assumption that no pain will cover an area larger than two window diameters and the patient delay time will not be greater than the time required for the gantry to travel through three windows. In addition, adding more than three windows to a series vastly increases the complexity of the algorithm. The algorithm developed can be broken down into the following 3 simple to follow and understandable cases which try to both (a) determine the unknown delay time and (b) reduce pains that cover areas larger than one window. The logic of this algorithm is based on an "ideal patient" who has no variability in his/her delay time at any given location. However, variations in delay time and in the size of the painful area between sites is accounted for by keeping each series of windows independent from one another.

CASE 1: Presses in the first window.

SITUATION 1.1: Single Window.

STEP 1.1.1) When the pain button is pressed in an area where no previous windows exist, a window of operator selected diameter and 0% power is established behind the gantry position at the time of the press (Figure 12). This window is established in order to attempt to alleviate the pain the ultrasound has caused and to account for the delay time between the position of the gantry when the pain was felt and the position of the gantry when the button was pressed. A typical scan speed of 40 mm/sec and the default window diameter of 20 mm allows for a maximum of about 0.5 seconds for the delay time of the patient. Future presses in this window control power in this window.

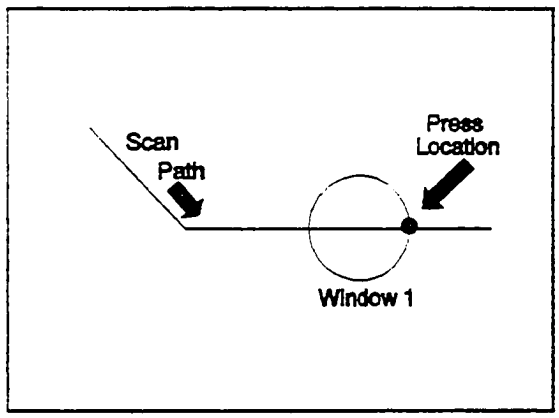

Figure 12. First Window.

STEP 1.1.2) Once a window is established, the program will search for the magnitude of power that can be delivered inside this window without causing pain to the patient, i.e. no further pain button presses are made within the window. This is done by

automatically increasing the percentage of window power in the controlled window by 10% with each pass through the window up to a maximum value of 90%.

STEP 1.1.3) If the pain button is pressed a second time when the gantry is inside of the controlling window, the assumption is made that the power has surpassed the patients tolerance in the window being controlled. The power will then be lowered in the controlled window by 10% and then be held there unless there is another press in the controlling window, in which case the power in the controlled window would be lowered an additional 10% and held at this level. This process can be repeated until 0% power is reached. The logic followed for future presses in this window when it's power is at 0% is covered below.

SITUATION 1.2: Double Windows.

STEP 1.2.1) The patient could at sometime press the pain button in the controlling window while the power is at 0% in the controlled window. This could occur if the patient delay time was greater than 0.5 seconds or the area that caused pain is larger than one window diameter. When this

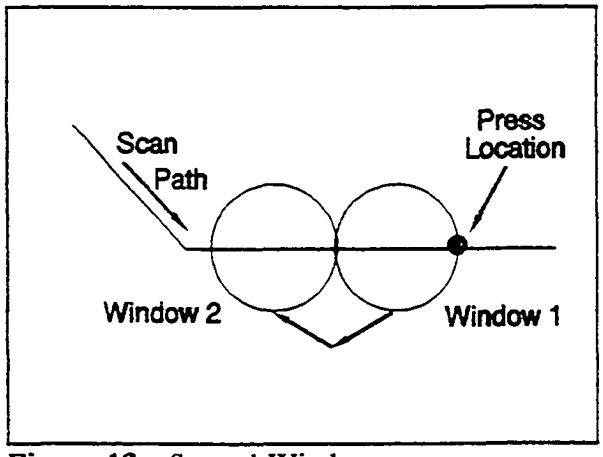

Figure 13. Second Window.

happens, a second window with 0% power is established behind the first whose power is controlled by button presses in the first window. This is shown in Figure 13 where the arrows below the windows indicate that presses in window 1 are controlling the power in window 2.

STEP 1.2.2) Windows 1 and 2 will start increasing in power in the same manner as described in steps 1.1.2 and 1.1.3 in order to determine the patient's tolerance. Both window powers are grouped together at the same power because the patient's delay time might be less than the time required for the gantry to move through one window and the pain area might overlap both windows as shown in Figure 14. This is a compromise in the conservative direction in the face of uncertainty about the delay time of the patient and the size of the pain region. It should be noted that future algorithms should try to more thoroughly deal with this situation.

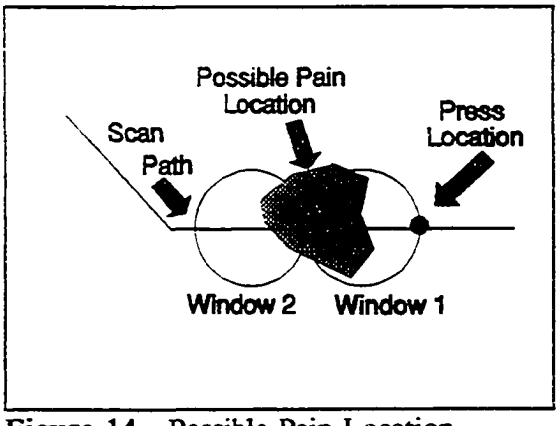

Figure 14. Possible Pain Location.

SITUATION 1.3: Triple Windows.

STEP 1.3.1) If the patient delay time was longer that the time required for the gantry to move two window diameters causing the pain to persist with two windows (indicated by a press when the gantry is in the first window while the power in the first and second windows are 0%), a third window with 0% power is established behind the second (Figure 15).

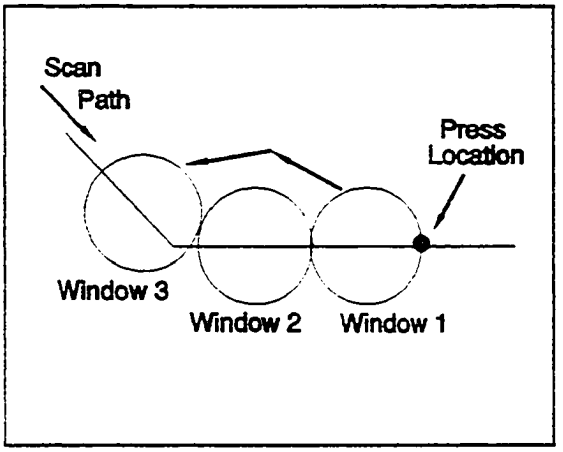

Figure 15. Third Window Location.

STEP 1.3.2) The power in window 3 then increases in the same manner as described in step 1.1.2 and 1.1.3. The arrows between windows 1 and 3 in Figure 15 are to show that the power in window 3 is being controlled by presses in window 1 in the same manner as described before. The power in windows 1 and 2 are reset back to 100% since they were ineffective. It is assumed here that the patient delay time is being searched for because the search for the size of the pain area was not effective. This is the one exception to the general rule of having pain button presses lower the ultrasound power. The exception was made because three windows in a row with low power settings would prevent major portions of the target volume from being heated.

STEP 1.3.3) Assuming the patient delay time is known and that the pain covered an area larger than one window diameter (as indicated by a press in the first window while the power in the third window is 0%), the power in the second window is again reduced to 0% in order to cover the area of pain that the third window did not cover. The second and third window powers are then controlled by presses in the first window in the same manner as described for step 1.1.2 and 1.1.3.

SITUATION 1.4: Complications in the above steps.

STEP 1.4.1) The first complication occurs in step 1.2.1 when there is a pre-existing window of a different series and 0% power behind the first. Since there would be no benefit in establishing a window at a location that is already at 0% power, the "second" window is established behind the pre-existing window (Figure 16). The arrows between windows 1 and 2 in Figure 16 indicate that presses in window 1 are controlling the power in both windows. The power setting of windows 1 and 2 shown in Figure 16 are set as was described in step 1.2.1. If the pre-existing window from the different series has a power setting greater than 0%, then the "second" window is established on top of the location of that pre-existing window. This situation is then the

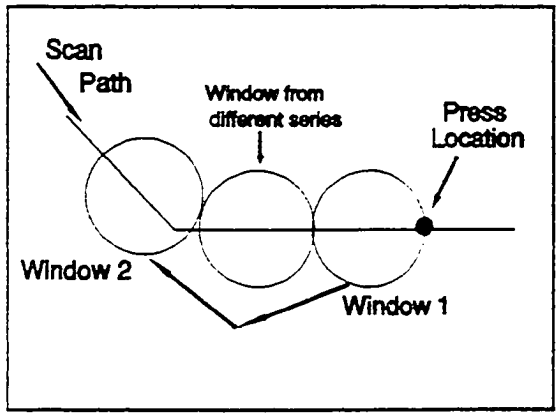

Figure 16. Second Window with Pre-existing Window.

same as step 1.2.1. It is then possible for the gantry location to be inside of more than one window (i.e. the area where windows are overlapping in Figure 17). When this happens, the gantry is considered to be in whichever window has a lower power setting. This conforms to the overall conservative approach used in setting power levels.

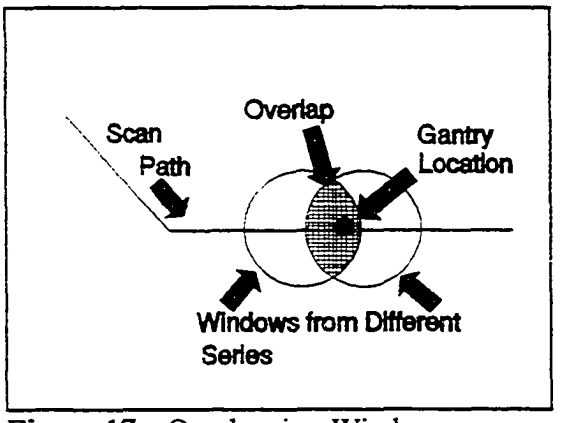

Figure 17. Overlapping Windows.

STEP 1.4.2) The second complication occurs from a similar situation that can occur when the program is establishing window 3 in step 1.3.1. The power setting of windows 1 and 2 shown in Figure 18 are set as was described in step 1.3.1. The program looks behind the second window to see if a window from a different series and 0% power has already been established there. If such a window is found the third window is established behind it (Figure 18) for the same reasons given in step 1.4.1. It is then possible for the gantry location to be inside of more than one window (i.e. the area where windows are

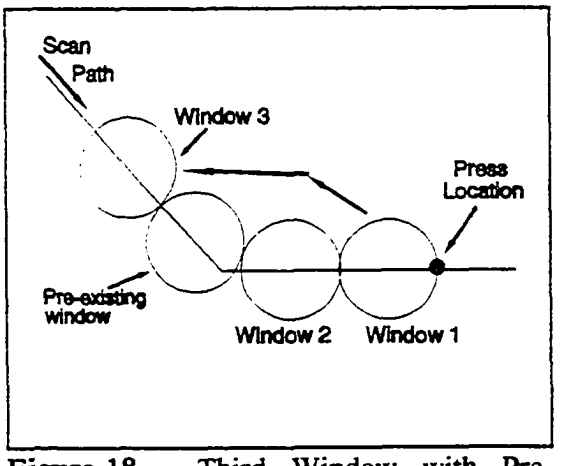

Figure 18. Third Window with Pre-existing Window.

overlapping in Figure 17). When this happens, the gantry is again considered to be in whichever window has a lower power setting.

CASE 2: Presses in window 2

STEP 2.1) If a button press occurs in a window whose power is being controlled by presses in a different window it starts a new series. Pain button presses can then arise in one of two different windows. The first window that the press could occur inside of is a "window 2" that is controlled by presses in a "window 1" as shown in Figure 19. Such "windows 2's" can arise from the conditions that created either Figures 15 or 17. The logic controlling the new series of windows is started from step 1.1.2 where the power in the new window is controlled by presses in the old window 2 as shown by the arrows between the windows in Figure 19. The power settings of the windows from the old series are not altered.

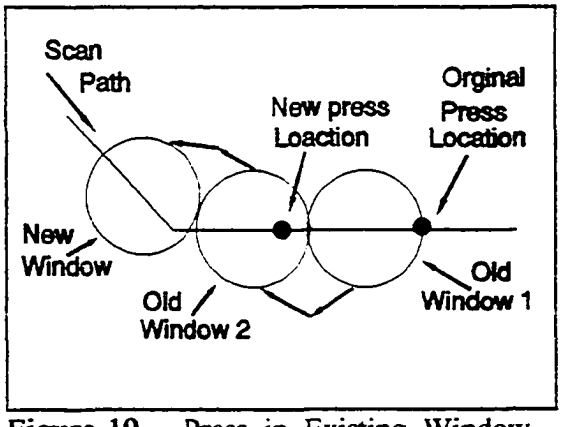

Figure 19. Press in Existing Window - Part 1.

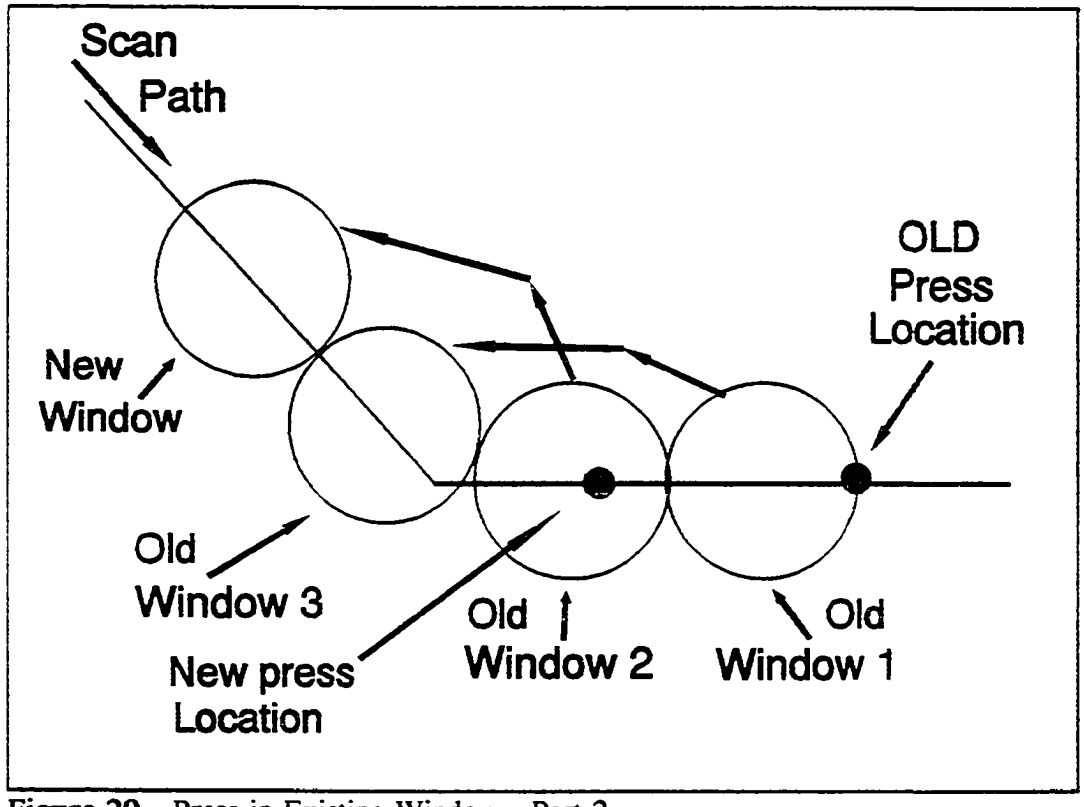

Figure 20. Press in Existing Window - Part 2.

STEP 2.2) The next possibility is that the a pain button press occurs in a "window 2" of Figure 16 or 18. In this situation the new window would be established behind the old window 3 (Figure 20). The new window would then be controlled by presses in the old window 2 as shown by the arrows in Figure 20.

CASE 3: Press in window 3.

STEP 3.1) If a press occurs in a "window 3" of Figure 15 or 18, it is handled in the same manner as shown in Figure 19 with old window 2 replaced by old window 3. The power in the new window is then started from 0% and increases in the same way as described in steps 1.1.2 and 1.2.3.

Figures 21-23 show a flow chart of the complete algorithm.

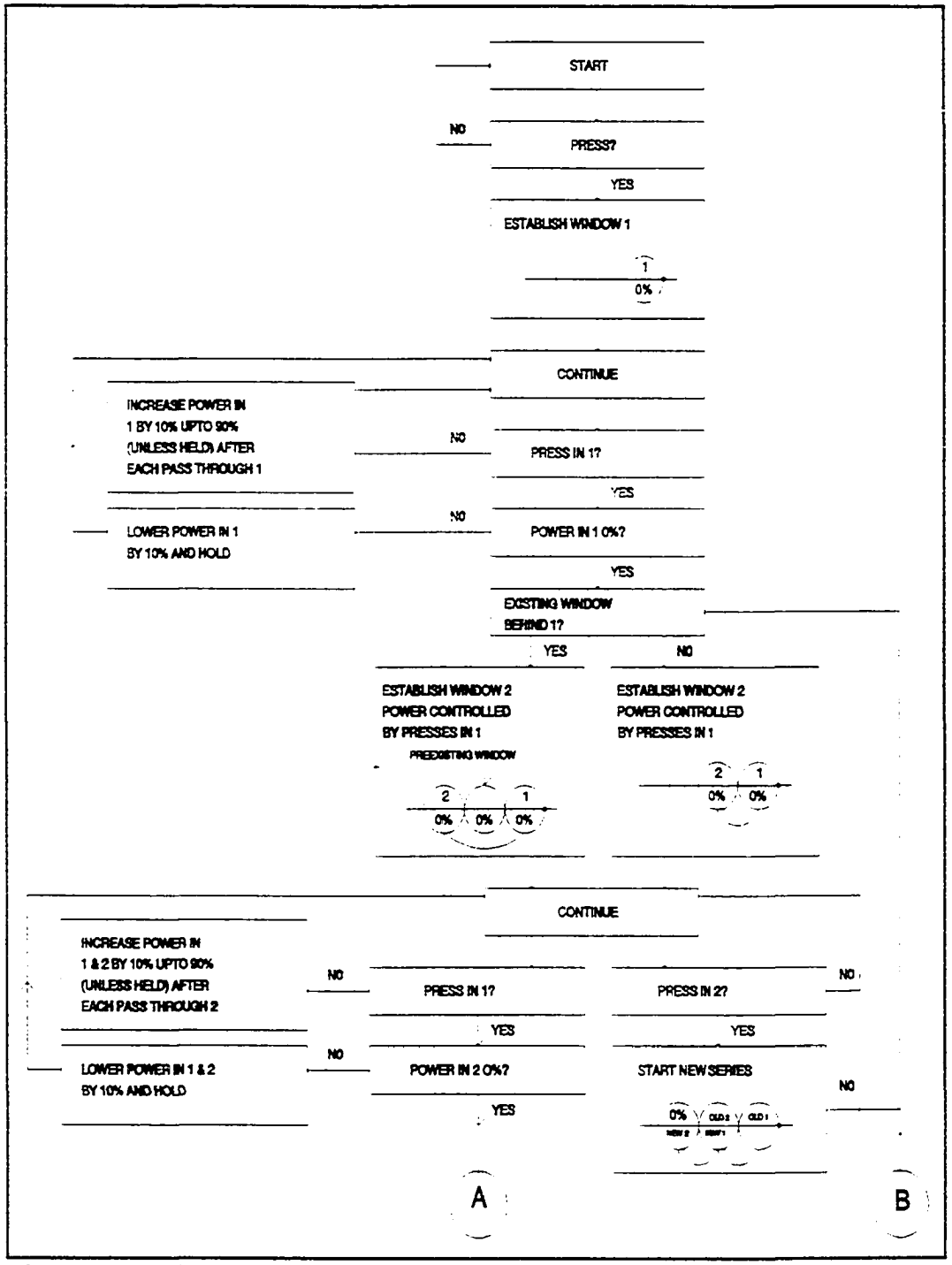

Figure 21. Pain Button Algorithm - Part 1.

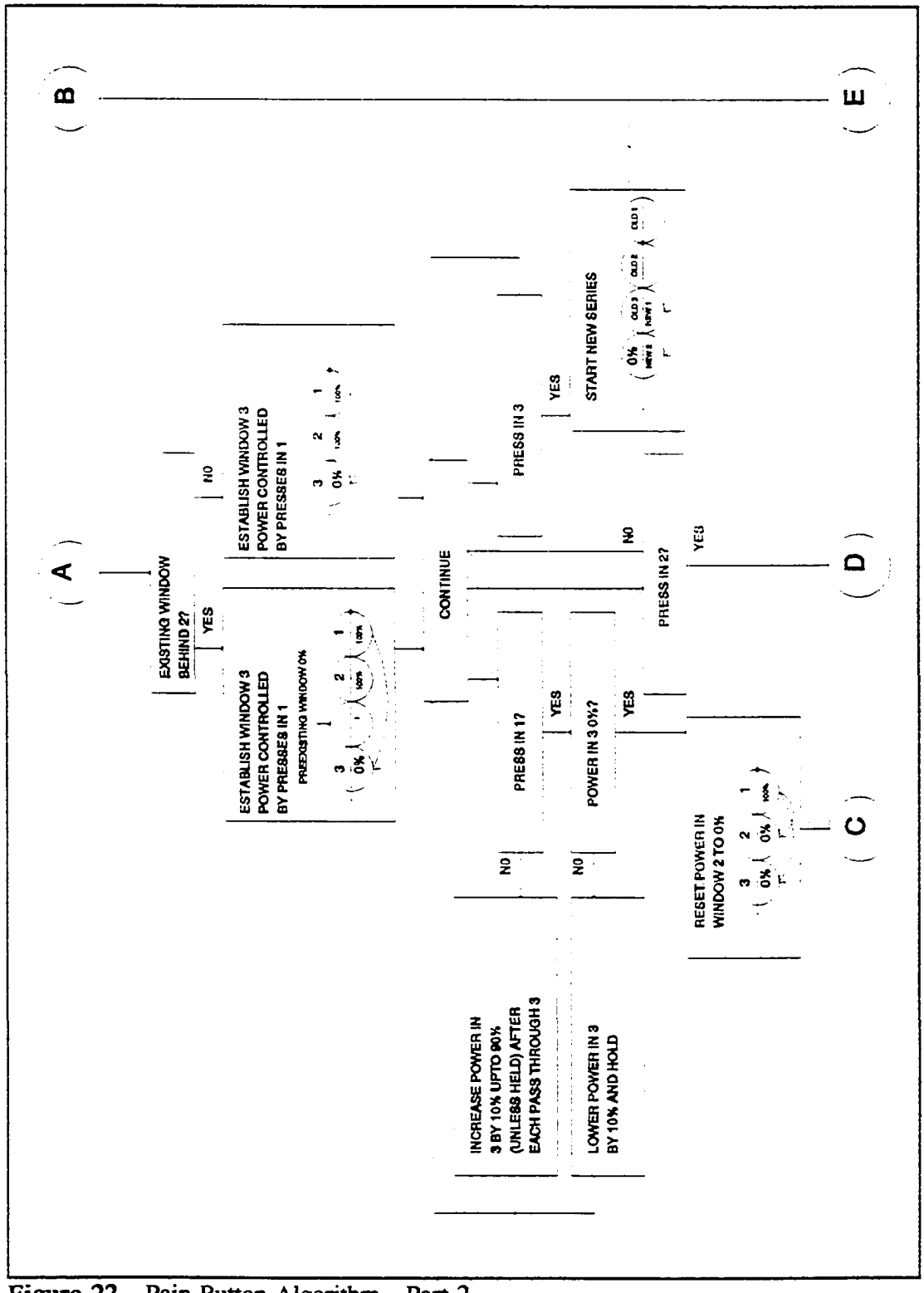

Figure 22. Pain Button Algorithm - Part 2.

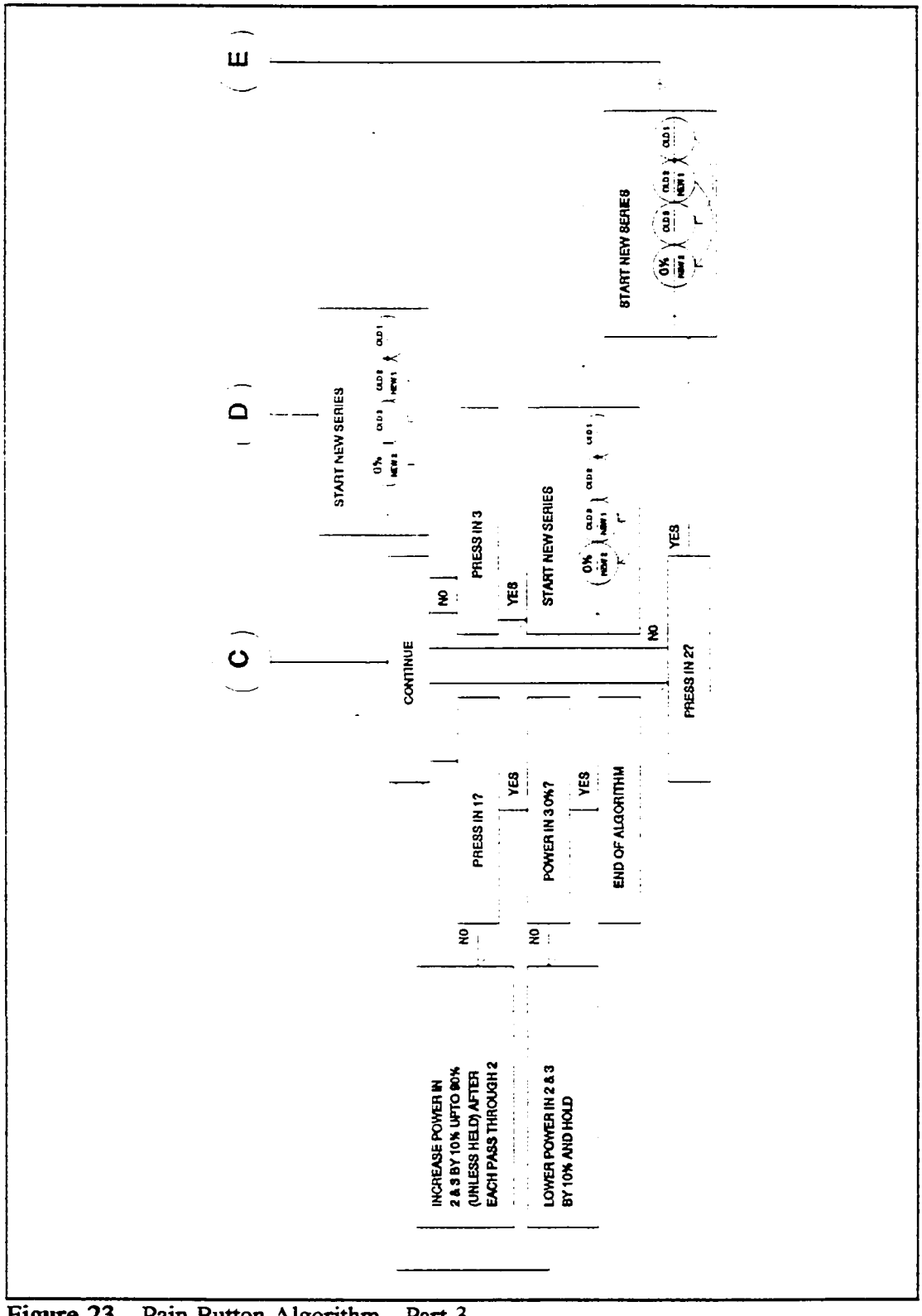

Figure 23. Pain Button Algorithm - Part 3.

2.5.2 PAIN BUTTON OPERATION

When the pain button is pressed (signified by a BEEP from the computer), a circle will be drawn on the screen behind the location of gantry at the time of the press creating a pain window (shown in Figure 3 as a circle just below the gantry position). The pain button is debounced both in hardware and software. The hardware debouncing consists of a capacitor across the switch contacts. The software debouncing requires that one second must elapse between button presses.

The diameter in millimeters of a pain window is selected by the operator. The physical size of the window on the screen is dependant on the screen scale which is adjusted manually by zooming the size of the screen and automatically by the program. When first created, the circle defining the window will be red. A circle that is all red signifies that the ultrasound power will be 0% of the sector power whenever the gantry position is inside. As the gantry passes in to and out of the pain window, and more pain button press occur inside of the window, the percentage of power will change both up and down. How the power changes in response to these events is dictated by the pain algorithm detailed previously.

As the percentage power changes, the circle will change from red to white. The amount of white on the circle is proportional to the percentage of power inside of the window it is defining. This allows the percentage of power inside of a window to be read like the hand of a clock. Thus, a circle that is half red and half white would be at

50% power. The power percentages are in 10% increments which translates to 36 angular degrees on the circle per 10% change in power.

2.5.3 PAIN BUTTON HARDWARE

The pain button is a momentary contact, normally open switch mounted atop two small batteries. When the switch is closed by the patient, current is sent along a cable into the duty cycle box where it lights a LED. A photo detector senses when the LED is illuminated. The electrical isolation provides the patient with a safe method for interfacing with the hardware. The output of the photo diode is amplified to TTL levels and monitored by the digital input of the Vectra's 2801 I/O card. Appendix C contains a complete schematic of the pain button along with all of the appropriate pin outs.

CHAPTER 3.0: EXPERIMENTS / RESULTS

3.1 PROGRAM VERIFICATION

The correct identification of gantry scan parameters is critical to the proper operation of the program. Table 1 lists the verifications that were made of the scan identifications that occur in a treatment.

Automatic scan identification correctly determines the scan size and gantry speed
Correct determination of inner/outer scan throughout the treatment
Screen automatically zooms when gantry bumps the edge of the graphics display
The first scan center aligns the tumor trace and thermocouple locations

Table 1. System/Program Checks for Scan Parameter Identification.

A graphical display of treatment parameters is only useful if it contains accurate information. To this end, Table 2 contains the checks made to ensure that the display of the scan information is correct.

The displayed position of the gantry location is correct relative to all other scan information
Inner sectors 8-12 are only displayed if an inner scan exists
Movement of the center of the scan is correctly displayed
Sector lines are not allowed to overlap
Thermocouple temperatures that are out of the screen scale are not displayed unless they are selected for use by the controller
Thermocouples are displayed in the correct locations
Thermocouple colors and arrows are displayed correctly
Thermocouple temperatures are only displayed when in the valid range of values
Tumor trace data filters only allow entry and the display of appropriate data
Trace is displayed with the correct scale regardless of how the screen is zoomed

Table 2. Display Checks from Dog Trials.

Table 3 lists the items that were verified in order to ensure the correct entry and use of thermocouple information because the temperature data is vital in the use of the temperature controller.

Individual target temperatures for temperature controller are used for correct sector
Thermocouples are assigned to the correct sectors
The thermocouple with the highest ARMA is correctly identified for each sector
Thermocouples that are disabled by the user are not displayed on the screen and are ignored by the controller

Table 3. Thermocouple Information from Dog Trials.

Table 4 lists the checks required to ensure that the ultrasound power is adjusted as specified by the program.

Sector lines act as power boundaries
Manual adjustment of sector power sets power for the correct sector
Power selections made by the temperature controller for each sector changes the power in the correct sector
The power in sectors with no thermocouples is not adjusted by the temperature controller

Table 4. Power Checks from Dog Trials.

3.2 EXPERIMENTS

3.2.1 DOG EXPERIMENTS

The initial verification of the hardware and software constructed for this work was accomplished during the treatment of 13 patient dogs. The patient dogs were selected by local veterinarians as candidates for anti-cancer treatment and then referred to the Cancer center for evaluation. The dogs were treated with SFUS hyperthermia if they were considered to be treatable by this modality. These treatments demonstrated that the construction and implementation of the hardware used was correct and that no program or system errors were present. The dogs trials also validated the correctness of new

features outlined below and explained in the users manual located in Appendix A. Finally, they provided invaluable experience in the operation of the SFUS system used at the Cancer center.

3.2.2 PATIENT TREATMENT

After the correctness of the system was verified it was used for the treatment of a patient. The patient was selected from those normally treated with SFUS at the University of Arizona. The criteria used for patient selection was the size and location of the cancer being treated. In the case of the patient data presented below, the cancer covered a large area and was located on the chest wall with a more or less uniform thickness. The patient provided the basis for continued study with the system developed.

3.3 TEMPERATURE CONTROLLER

The dog treatments discussed above also served to analyze an initial PI controller with successful results. The protocol followed for the use of the controller was: During a patient treatment the manual power control is initially used to adjust the overall power until the desired temperature is achieved or, the patient's pain tolerance is reached. When the overall power has not been altered for approximately fifteen minutes and the temperatures trends in the treatment area have reached a steady state condition, the sector lines are manually adjusted to separate hot and cold areas of the scan into separate

sectors. Any thermocouples that the operator does not which to be used for control are deactivated at this time as per Appendix A 3.12. The controller is then activated concurrently with an increase in overall power of about 10% in order to give the controller room to operate. The controller is then permitted to control the power in each sector that has thermocouple representation. Power changes to all sectors, as determined by the PI portion of the controller, occur with each reading of the temperature field at 30 second intervals. The power in sectors without thermocouples is not altered.

As a result of the dog treatments and after subsequent evaluation of everything learned, the PI controller was replaced with the PID controller described previously which has been extensively evaluated for stability and response characteristics by Lin et al. 1990 and by Lin 1990. (The addition of a derivative term to a PI controller will serve to improve the stability of a system and increase damping [Franklin et al. 1991].) The primary modifications to Lin's PID controller include the bumpless transfer from manual to automatic control, computer selection of the maximum ARMA temperature for input into the controller, and manually adjustable sectors that assign the thermocouples to different regions.

3.4 TEMPERATURE CONTROLLER RESULTS

Figure 24 shows temperature plot for all thermocouples in the tumor during a successful dog treatment which used the PI controller. The controller was activated at 58 minutes and deactivated at 77 minuets.

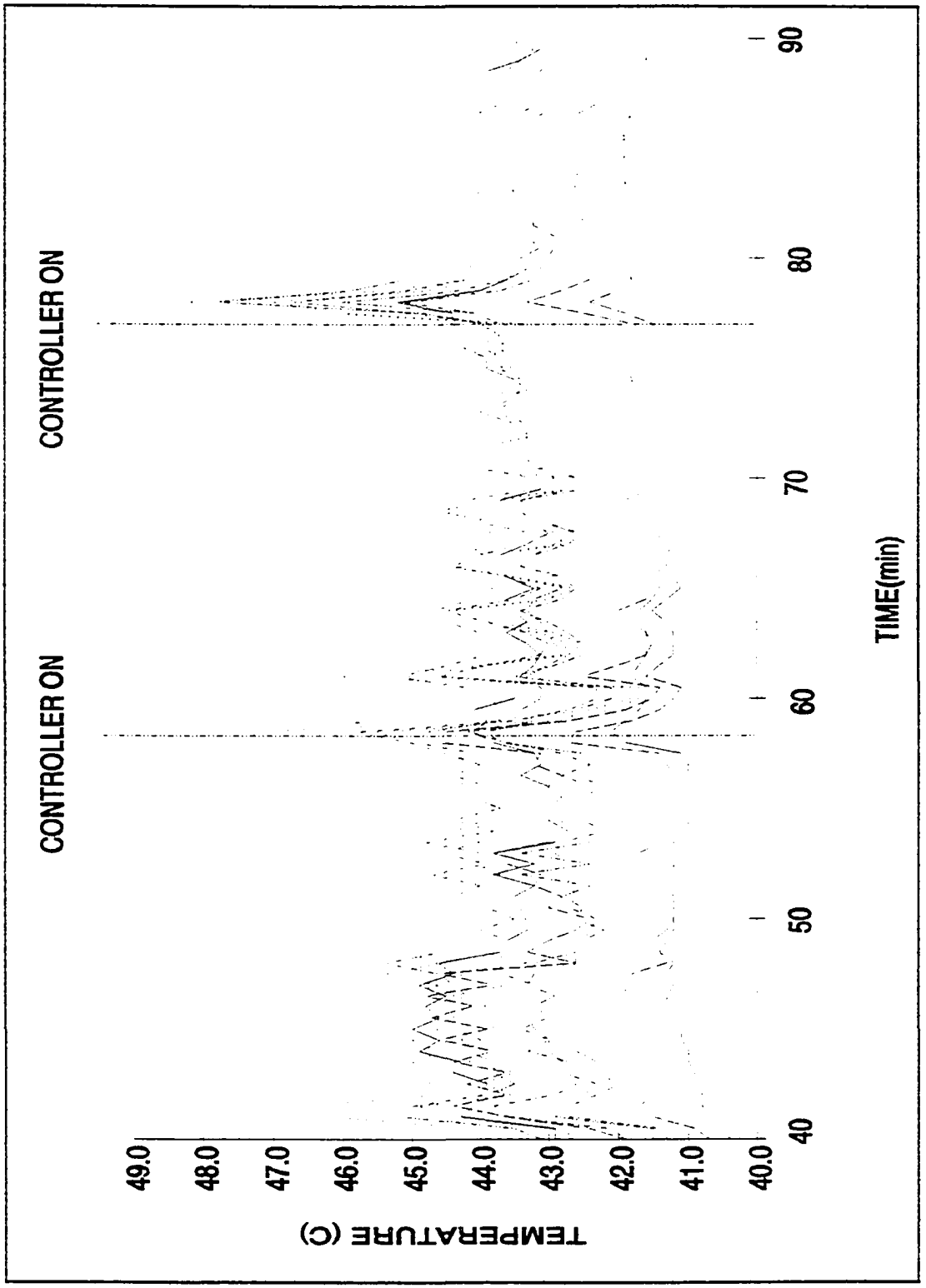

Figure 24. Successful use of PI Controller.

The PID controller has been used on one patient for two consecutive treatments with results given below. More clinical results will be obtained later after a faster 486 computer is tested and replaces the Vectra 386 computer.

An example of the PID controller used on a patient is shown in Figure 25 (the controller was turned on at 25 min). In this treatment the transition to control from manual operation did not use the error initialization described above (bumpless transfer), and the resulting dip is seen in Figure 25.

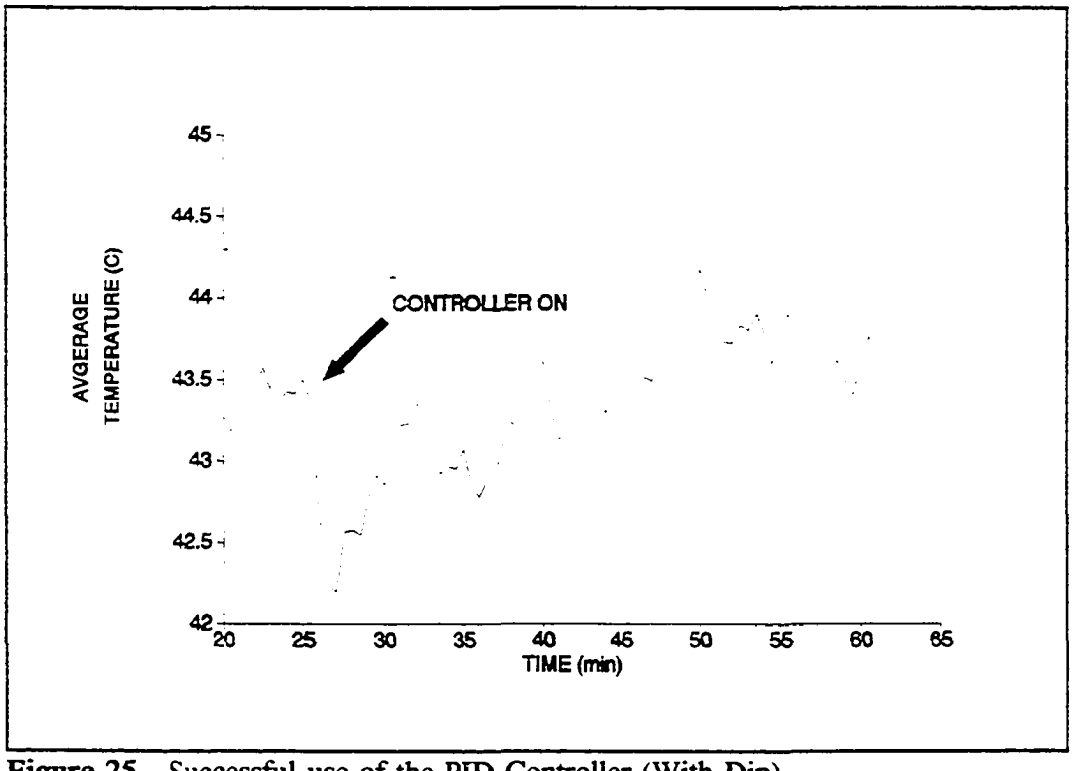

Figure 25. Successful use of the PID Controller (With Dip).

The next treatment to the same site of the same patient in Figure 25 is depicted in Figure 26 with the addition of the error initialization to the controller (equation 5), creating a smooth transition to computer control. Figure 26 also shows improvement in the uniformity of the temperature field when the controller is activated with a target temperature of 43.0 °C and a time of 39 minutes. Power previously to the activation of the controller was at 100% in all regions in this treatment.

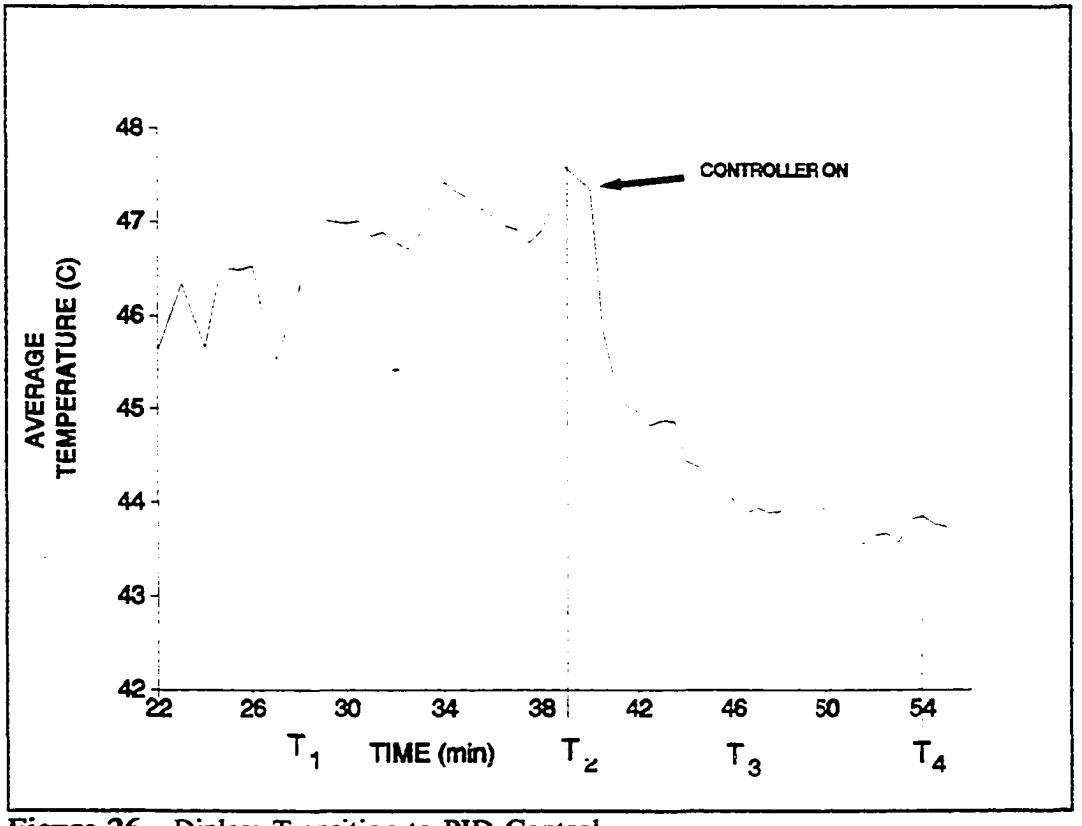

Figure 26. Dipless Transition to PID Control.

The uniformity of the temperature field can be measured by the variance of all of the temperature probes in the tumor. Figure 27 shows that the variance dropped during the second treatment from approximately 8° C to 2° C, which is a significant improvement.

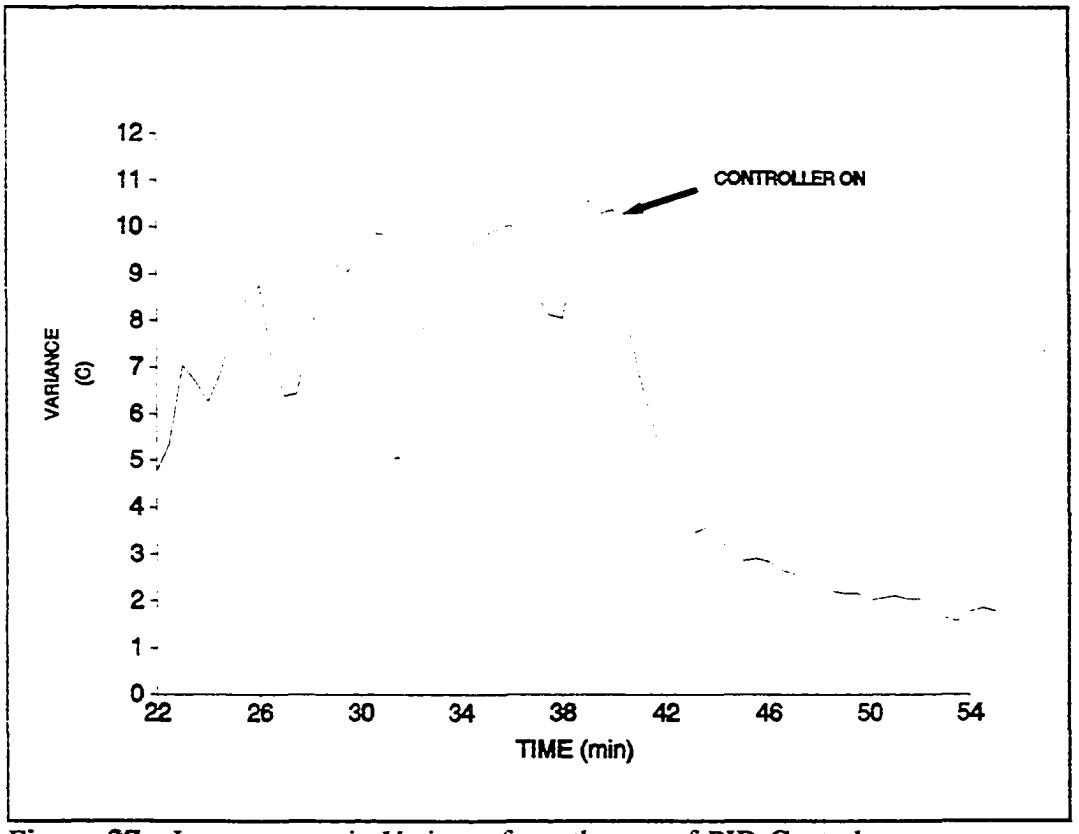

Figure 27. Improvement in Variance from the use of PID Control.

The two histograms in Figure 28 show the percentage of probes above a given temperature. The histograms were constructed from averages of all of the temperatures of thermocouple in the tumor during manual control (from T_1 to T_2 in Figure 26) and after (from T_3 to T_4 in Figure 26) the controller was activated.

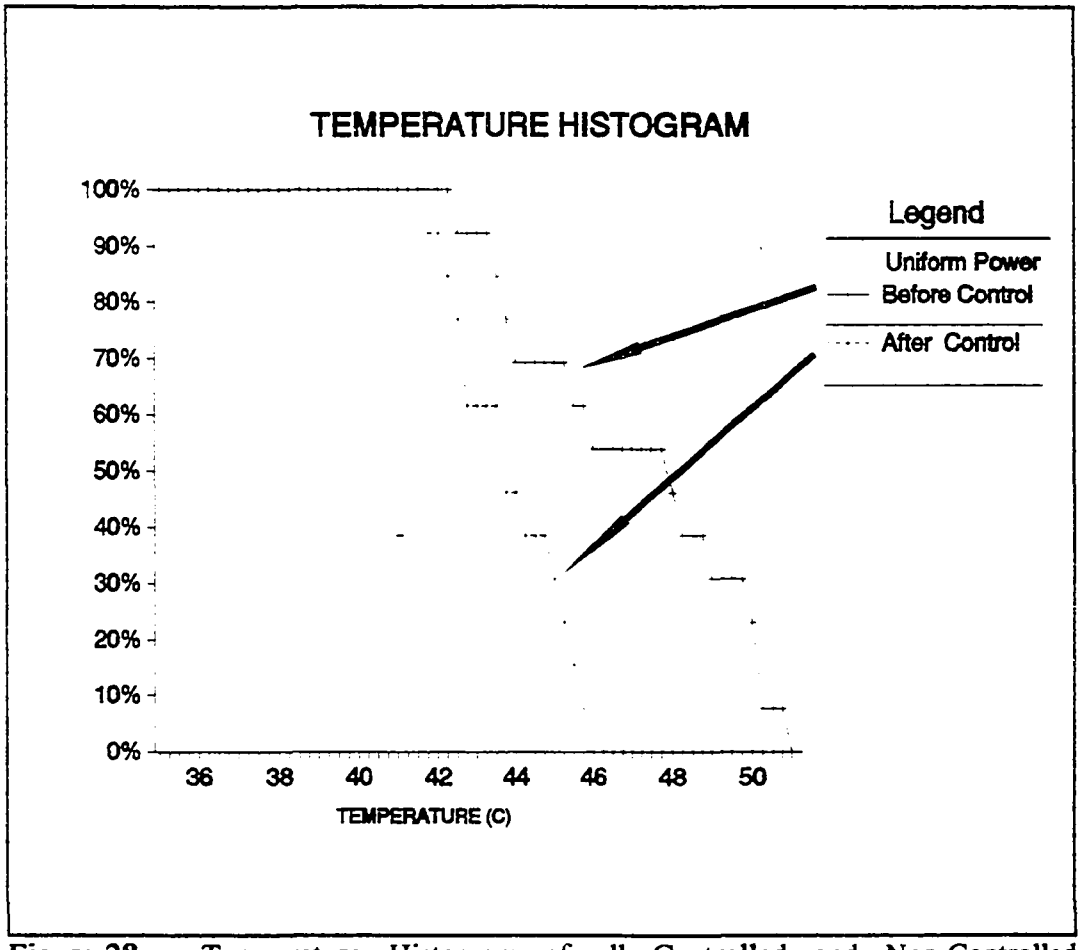

Figure 28. Temperature Histogram of all Controlled and Non-Controlled Thermocouples in Tumor.

Figure 29 displays the maximum ARMA filtered temperature input to the controller for each sector that contained thermocouples. The numbering and angular arrangement of the sectors was shown in 3.

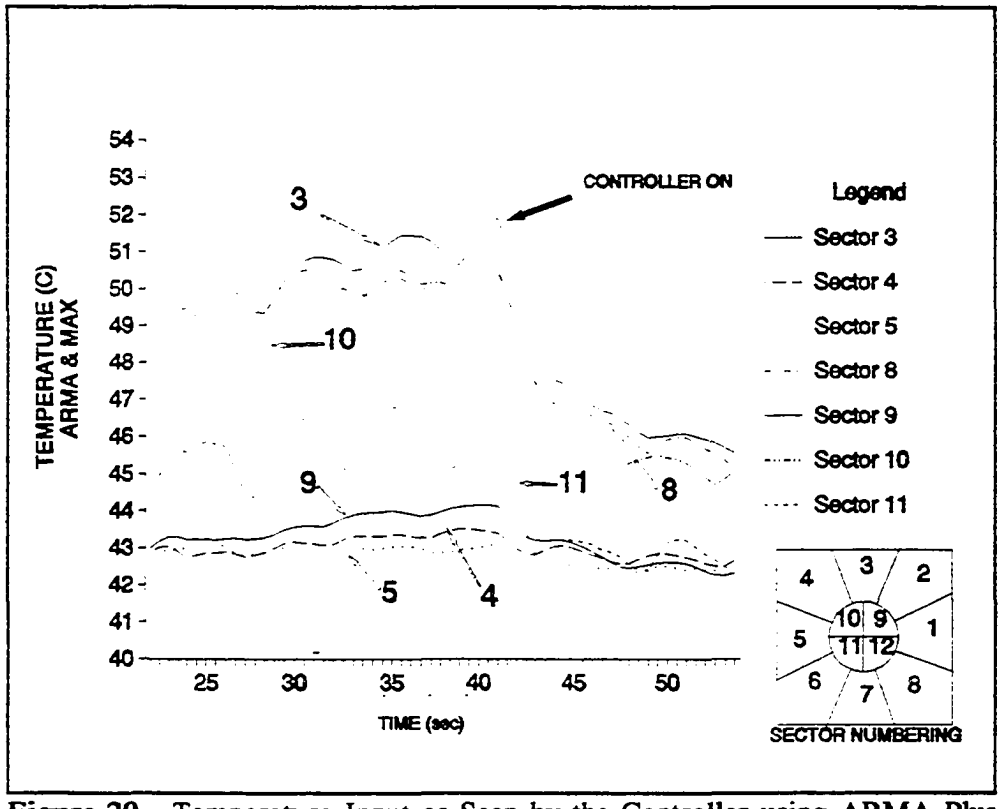

Figure 29. Temperature Input as Seen by the Controller using ARMA Plus Max Temperature.

3.5 PAIN BUTTON

For verification of the pain button system and accompanying software a series of tests were performed on both the old algorithm described in Appendix B and the new algorithm presented in section 2.5. The tests (listed Table 2) showed that the pain button operated according to the algorithm described above and behaved as expected in the various circumstances that occur during a patient treatment.

The start of a new scan resets all windows
Pain button software debouncing only accepts valid presses
Button press establishes a window behind the gantry location at the time of the press
Power in a window is at 0% during the first pass of the gantry through the window
Power in a window increases by 10% with each subsequent pass through the window
Power for a window is not permitted to increase past 90%
Power in window is reduced by 10% with additional presses and held
Power in a window stays at its held value
Window follow all steps of the pain algorithm
Absolute ultrasound power changes when the gantry enters a window and returns when the gantry exits
Absolute power is a window is a function of sector power
Absolute ultrasound power changes while the gantry is in a window and the gantry enters a new sector of a different power setting
Gantry position is taken to be in the window of lower power if two or more windows overlap
Windows stay in the correct position when screen scale is changed

Table 2. Pain Button Checks.

After the above verifications, the pain button with the old algorithm was clinically available over a period of two years. Whenever a patient was to be treated with SFUS the operator of the system would decide if this treatment had the potential of being painful for the patient. The decision was based on the operator's past experience with similar treatments or on the patient's own treatment history, if one existed. Deciding factors included the tumors proximity to bones and the amount of medication

administered to the patient prior to treatment. From the operators standpoint, the button was given to the patient if they were experiencing sharp pain that appeared quickly and then faded in unison with the repetitive cycle of the gantry scan pattern. If the pain button was not initially given to the patient, it would be made available if the patient experienced pain. The pain button was always given to the patient with the explanation that pressing the button would allow a computer to help alleviate the pain. The patient was also told that the button should be pressed as soon as sharp pains are felt.

3.6 PAIN BUTTON RESULTS

The pain system described in section 2.5 was an evolution of schemes. The immediate predecessor to the one above is described in appendix B, and can be summarized in three steps. A- Establish a window and look for the correct power. B - If step one fails, move the location of the window back one radius. C- After three executions of step B, the diameter of the window is enlarged up to a maximum of 150% of its original size. The algorithm just outlined was available during the treatment of 28 patients over a two year period for a total 84 treatments. During these treatments, 65 complaints of unbearable / excessive temperatures or pain were made. Out of the 65 treatments, 26 of the patients experienced (and were able to identify) the sharp cyclical pain that the pain button was designed to help alleviate. Data collected during the 26 treatments consists of 850 pain button presses which are broken down in the pie chart in Figure 30. Moving the location of the window occurred in 17 (65%) of the 26 treatments

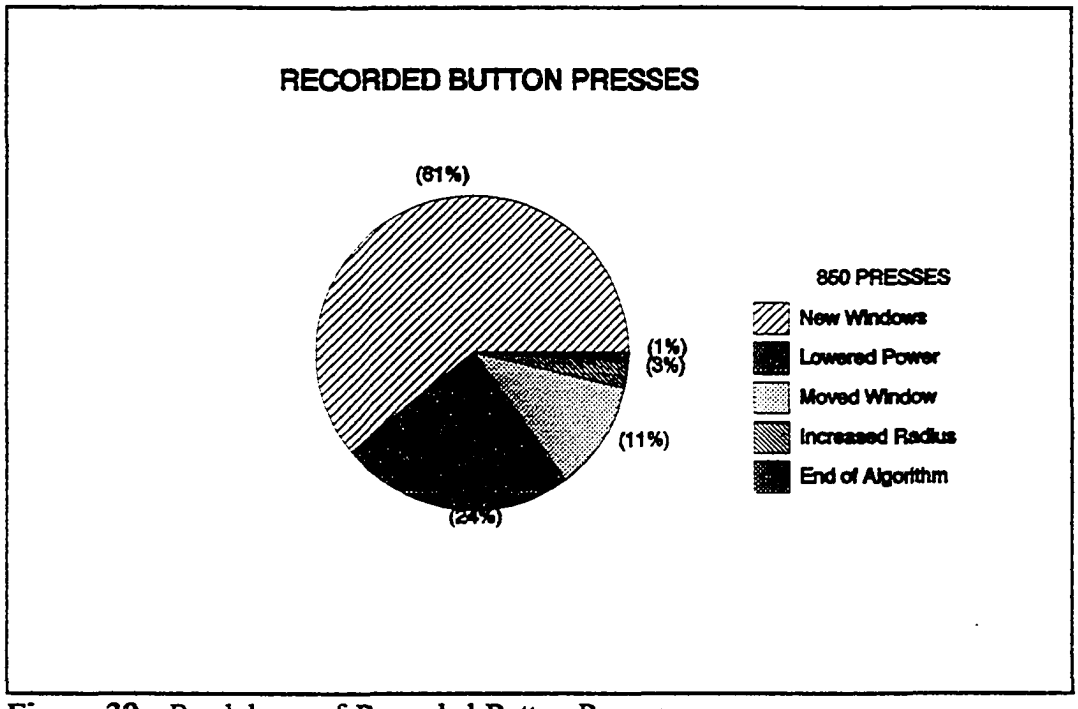

Figure 30. Breakdown of Recorded Button Presses.

in which the button was used. However, 95 (11%) of the 850 recorded presses with the old algorithm progressed of all of the windows established progressed to the point where the location of the window was moved.

A typical example of the pain button being used during a patient treatment is shown in Figure 31. The pain button was pressed a total of seven times establishing three separate windows. Before the pain button presses, the patient complained of sharp pain. All three of the windows progressed to step four of the algorithm explained in appendix B whereupon the ultrasound power was adjusted to 90% in windows one and two and to 10% in window three.

After analysis of the data collected and observation of the treatments in which the button was used, it was determined that the fifth step as described in appendix B created

a logic flaw in reasoning. The flaw was that the old algorithm did not account for delay times longer that the time required for the gantry to travel one window diameter or pain areas that were larger than one window diameter. The flaw is seen when the patient presses the pain button causing the pain window to be relocated. The patients tolerance for pain is not be found because the patient would eventually press the button near the first window location establishing a new window versus adjusting the power in the first window in its relocated position as needed by required by the patient. The first window in its new position would then progress past the patient's tolerance causing presses in the second window. The second window would also advance in the algorithm until it is relocated- starting the process over. It was for this reason that the algorithm was deemed to have not been entirely successful in effectively eliminating the patients pain for most of the treatments in which then relocation step was reached. Based on the above ratio, the logical flaw just

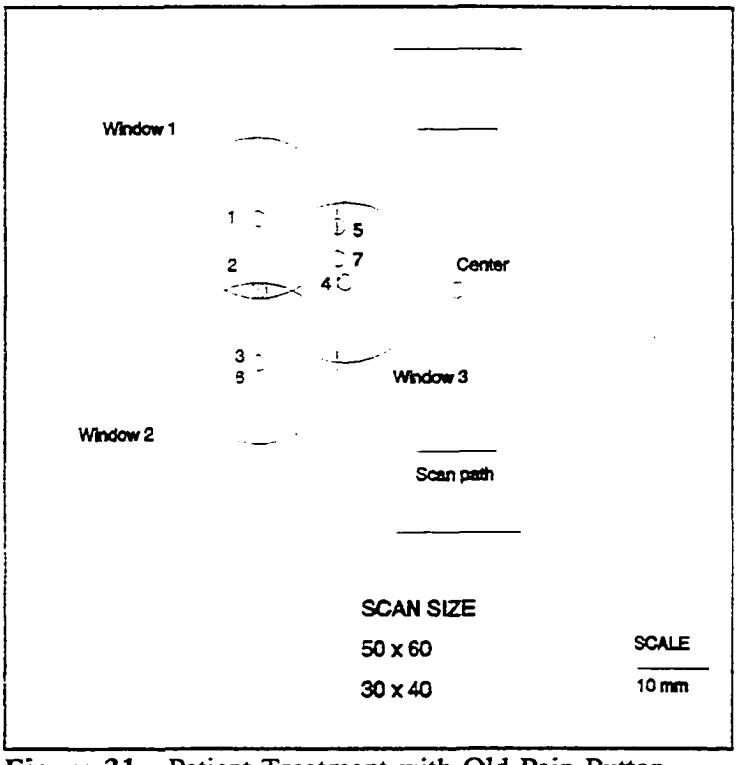

Figure 31. Patient Treatment with Old Pain Button.

described, and the operators own experience, the new algorithm presented above was designed and awaits clinical trials.

CHAPTER 4.0: DISCUSSION

4.1 TEMPERATURE CONTROLLER

The temperatures achieved with the addition of power control as a function of position could still be improved, but appear to be more uniform when compared to not having control as a function of position. In addition, the operator was not required to monitor and adjust the power level. It can be seen in Figure 24 that increased damping is required because of the oscillations in the temperatures seen during the operation of the controller. This shows the need for the derivative implemented for the next series of treatments and/or increased scanned scanning speed. In addition, initial treatments (like the one shown in Figure 24) during the use of the PI controller and the first patient treatment that used the PID controller (shown in Figure 25) contained dips in the temperature when computer control was first activated. This demonstrated the necessity for the bumpless transfer to automatic control that was outlined in section 2.4.2. The histogram (Figure 28) shows that the increase in temperature uniformity was not at a substantial cost in terms of the minimum temperature characterized by any area of the histogram to the left of the 43 C° line. In retrospect, it is apparent from the histogram of Figure 28 that the control temperature should have been set higher than 43 $^{\circ}C$. While it is not known what an ideal histogram would look like, an infinite slope at the target temperature is a good acceptable goal. The increase in the slope of the histogram (caused by activating the controller) also reflects the lowering of the variance seen in Figure 27.

Figure 28 shows that the temperature controller did what was expected- control the power in such a way as to increase the uniformity of the temperature field. Figure 29 (the controller input with arma and max) shows that the temperatures settled into two groups, those around 42.5 C° and those around 45 C°. It can be seen that the power required to maintain the sectors at 42.5 C° prevented the temperature from decreasing in the hotter sectors. The power level for the hotter sectors was set at 0% after the 45 minute mark by the controller and the temperatures still did not fall. The power in the colder sectors settled to 100% power at the same time. This shows that all temperatures decreased when the controller was activated. It can be concluded from such variations that thermal coupling, acoustic coupling, the effects of the boundary conditions, or the effect of variations in the depth of the temperature probes existed between adjacent sectors (because the controller saturated to it upper and lower limits in all sectors it was controlling) these factors and should not be ignored in future controller designs.

4.2 PAIN BUTTON

Ideally Figure 30 should show that 50% of the recorded presses established new windows of the correct size to cover the area of pain and correctly accounted for the patient delay time. The other 50% of the recorded presses should lower and hold the power at the patients tolerance for pain. While a 50/50 split did not occur in the recorded pain button presses, the pie chart of Figure 30 shows that the old pain system recorded 61% of the presses as establishing new windows and 24% of the presses as

stopping the power from increasing and lowering the power in existing ones. This shows that the button is useful during treatments.

Figure 31 shows that the patient was able to consistently identify the area of discomfort by the use of the pain button. While the patient continued to indicate discomfort, the relief provided by the pain button alleviated the need to move the scan away from the center of the tumor volume.

Overall the pain button system has been shown to be beneficial during SFUS treatments. The different types of pain sensations (skin and deep) that were discussed in chapter 1 are no longer relevant to the operation of the treatment because the successful identification of pain in this system is only dependant on the time at which the pain occurs. For the same reason, the deep pain referral discussed in chapter 1 will not adversely effect the pain identification because the computer knows the location of the ultrasound gantry at the time of the pain button press.

CHAPTER 5.0: FUTURE WORK

There are many possible extensions to this work. This could include improvement of the controller by further eliminating integrator windup by imposing a second restriction on the evaluation of the integral of the error. This condition would only integrate the error when the power level is not saturated at either of its limits. Such a condition would prevent the area under the integrator term from growing in magnitude when no additional changes in power could be taken in the direction required to zero the error (Franklin et al. 1991). Another way to avoid windup is to implement a velocity form of a PID controller in which the proportional term depends on the derivative of the error instead of the error itself (Astrom and Wittenmark 1984). To improve the temperature profile, the controller could be given more resolution by dividing the scan area into more sectors than presently used. A more sophisticated multi-input multi-output (MIMO) temperature controller could be developed that could use fuzzy logic, or adaptive control laws to replace the SISO PID controller. Also, an identification phase could be used at the start of a treatment to find which thermocouples are coupled to each sector of the scan.

Another approach toward improvement of the treatment is to have the program vary the frequency content of the ultrasound to determine which frequencies are most effective in raising the temperature field and which frequencies are causing patient pain. The use of multiple frequencies would allow adjustment while maintaining the total absorbed power at a constant.

The program could also be made more intuitive by an improved user interface other than the keyboard. This new user interface could include a mouse, light pen, or touch screen.

APPENDIX A.0: PROGRAM USERS MANUAL

A.1 APPLE COMPUTER PROGRAMS

The pain program communicates with two other computer programs. The first is the scanning program on the Apple computer. The Apple computer should run the program "TALK" which is identical to the program "XYOCTAGON5POTS" written by Dennis Anhalt (University of Arizona, Cancer Center, Clinical Engineer) except that "TALK" sends scan parameters to this program over a custom computer bus. It does not matter which computer program is started first as long as the pain program is started before the first scan is initiated. If the Apple runs old scanning programs the pain program will then not be able to identify any scan parameters or identify when the gantry is in an inner or outer scan.

When the scanning Apple computer starts a new scan, the center of the gantry display on the Vectra will automatically be updated similar to the MOVE CENTER command except that when the center is set in this manner, the pain program goes into an identification phase to search for scan parameters such as weather there is an inner scan, the sizes of the scans, and the speed of the gantry. A message will be displayed stating that this process can be aborted if there is no inner scan to identify by pressing the "SPACE BAR". During this time, none of the menu items will operate until the identification has been completed.

A.2 HP TEMPERATURE COMPUTER PROGRAMS

The second computer that the pain program communicates with is the HP temperature computer. The program to run on the HP temperature computer is #19:cont1osc if the 1 MHz oscillator is being used exclusively or #19:cont2osc if the 1 MHZ oscillator and one Wavetek are being used. THE ORDER IN WHICH THESE PROGRAMS ARE RUN IS IMPORTANT and running them in the wrong order will result in the HP temperature computer locking up and requiring a complete restart by pressing the SHIFT and RESET keys simultaneously. The pain program on the vectra MUST be run before the "Y" conformation is entered to the prompt "Is all this data entered correctly?" on the HP temperature computer and must continue to run as long as temperatures are being taken. See the section on ENTER TUMOR TRACE AND TC'S for more information on how these two computers communicate and for an important warning. Other programs may be run on the HP temperature computer but the pain program will not receive any temperature information preventing the controller from having any effect on the treatment and preventing any temperatures from being displayed.

TO START THE PAIN PROGRAM TYPE "STP" FROM ANY DIRECTORY ON THE HEWLETT PACKARD VECTRA QS/20 386 IBM COMPATIBLE COMPUTER. STP is a batch file that runs the program PAIN1.EXE in the directory BC.

THE PAIN PROGRAM WILL THEN PROMPT FOR THE PATIENT'S NAME. If ENTER is pressed without entering a name, the default name of TEST will be used. The patient name is used for the title of all data files. If a name is entered that has been used previously, the program will alert the user and prompt for a unique name.

A.3.0 PROGRAM MENU

There are two methods for selecting menu items: The first way is to press the "hot key" highlighted in red for each of the menu items. The pain program is not case specific, i.e. "Y" is the same as "y". The upper left portion of the screen will then prompt for the correct user input for that particular item. The second method for selecting a menu item is to use the cursor arrow keys to move the menu pointer (√ in purple) to the desired item and press ENTER. Again, the upper left portion of the screen will prompt for the correct user input.

The menu items are listed and described here in order of appearance.

A.3.1 QUIT: hot key = "Q".

Used to end the pain program. When selected, the pain program will prompt for a yes-no confirmation. Only a correct response of "Y" or "y" will terminate program execution at which time the operator is required to insert a disk to backup the data files created during the just completed treatment. The program asks which of the floppy drives (a: which is a 5 1/4 inch drive or b: which is a 3 1/2 inch drive) contains the

backup disk and then checks to make sure that the name is unique. If it is not the program requires that a different disk be used without files of the same patient name.

A.3.2 WINDOW DIAMETER 20MM: hot key = "D".

Used to change to diameter of the pain button windows. This selection does not effect windows that have already been established. Once selected, the "+" and "-" keys are used to increase or decrease the diameter in 2 mm increments. The default diameter of 20mm is shown here. The menu list will display the current diameter. The acceptable range for the diameter is from 10 mm to 98 mm. If either limit is exceeded the diameter will rollover to the other limit.

A.3.3 CONTROLLER TARGETS: hot key = "T".

If the temperature controller is ON, the "+" and "-" keys are used to increase or decrease all of the controller target temperatures for each sector by 0.1 C increments. Individual sector target temperatures are independent of one another and can be changed by moving the menu pointer to the desired sector and using the "+" and "-" keys in the same way as described above. The valid range for controller targets is from 20 C to 50 C. If either limit is exceed the target will roll over to the other limit. The initial default target temperature is 44.0 C.

A.3.4 ZOOM: hot key = "Z".

Used to change the scale of the gantry position display. The "+" and "-" are used to add or subtract 10 mm from the scale of the gantry position display screen. The scale can been read by the light blue grid on the screen which shows a 10 mm grid when there have been no temperature positions and tumor trace entered. When temperatures have been entered, the left and bottom edges of the display will show tick marks at 10 mm increments. The minimum scale is 20 mm or the size of the inner scan (if there one currently exists). The maximum scale is 300 mm. The scale will be automatically adjusted to a best fit after temperature positions and tumor trace have been entered. If the screen is zoomed in smaller than the best fit the thermocouple and sections of tumor trace that do not fit on the new screen scale will not be displayed. Also, if the gantry bumps an edge of the display area the screen will automatically zoom out 10 mm to accommodate.

A.3.5 CONTROLLER IS OFF: hot key = "C".

Indicates the current state of the temperature controller. This item is used to turn the temperature controller ON or OFF. Pressing "C" or ENTER when the menu selector is on this selection will toggle the controller on or off. The menu will then display will then toggle to CONTROLLER IS ON (or OFF). Each sector and its target temperature are independent from one another. The controller will turn ON if there have not been thermocouple locations entered with the ENTER TUMOR TRACE AND TC'S command but it will have no effect. When activated, the manual power control will no longer be

available as will be seen from the power percentages for each sector changing to a target temperature. Once on, every time the HP temperature computer takes a reading, the temperature in each sector that the controller is using for input will be circled in red and the percentage power for that sector will be updated. If a sector does not have any thermocouple in it, no power change will be made for that sector. IT SHOULD BE NOTED that if the screen is zoomed in with the ZOOM command to a scale smaller that the best fit scale that the pain program selected, the thermocouple at the edge of the screen which no longer fit with the new scale will not be displayed but will still be used by the controller unless they are deactivated with the VALIDATE command described below. If the controller tries to use a thermocouple for input to that is not displayed because of the zoom setting, the program will zoom out until the thermocouple is displayed. When the controller is turned off, manual control will be restored. The percentages displayed after the transfer from automatic to manual control will reflect the last power percentages that the controller set. This was done to try and achieve a "bumpless temperature transfer". The controller was designed for a sample rate of 30 seconds. A sample rate different than 30 seconds will result in undershoot or overshoot of the temperature profile. Therefore, THE HP TEMPERATURE COMPUTER MUST BE SET FOR A SAMPLE TIME OF 30 SECONDS IF THE CONTROLLER IS GOING TO BE ACTIVATED. The control law used is describe in detail in section 2.0.

A.3.6 REDRAW SCREEN: hot key = "R".

Used redraw the gantry position portion of the screen in the event of any "garbage collection". This item has no other effect on the execution of the pain program.

A.3.7 RESET WINDOWS: hot key = "W".

Used to erase all pain windows that have been established with the pain button. This option does not reset the count on the total number of button presses available. Requires a "Y" or "y" confirmation.

A.3.8 MOVE CENTER: hot key = "M".

Used to change the center of the gantry position display screen to the current gantry position. Requires a "Y" or "y" confirmation. The pain program's display of gantry position can be visualized as a sliding view area over the range of gantry motion with the center of this window defined by this command. The gantry position display will center on the gantry's location at the start of the pain programs execution by default. If this item is used after the tumor trace and probe locations have been entered with the ENTER TUMOR TRACE AND TC'S command, a small red circle will be displayed to indicate where the tumor trace center is now located relative to the new gantry center. This command is executed automatically just before the apple computer starts a new scan.

A.3.9 ALIGN TUMOR TRACE: hot key = "A".

This selection is used to align the tumor trace and probe locations to the current gantry location. Requires a "Y" or "y" confirmation. BEFORE EXECUTING THIS ITEM READ THE WARNING ON THE ENTER TUMOR TRACE AND TC'S COMMAND. The only time this item should be used manually is when the alignment of the gantry center to the trace center is determined to be incorrect, i.e. if the patient moves or the apple was not started with the scan center aligned correctly to the tumor center. This command is automatically executed when the first center is established either by the MOVE CENTER command or by the first scan initiated by the scanning apple. This selection also executes a MOVE CENTER command described above.

A.3.10 ENTER TUMOR TRACE AND TC'S: hot key = "E".

When the this command is selected, a tablet self test is performed. If the self test fails, the command is aborted. The tablet is then configured in a remote request mode to allow the pain program to acquire data at its own rate. If the default configuration of a stream mode is used, the data quickly overflows the serial buffer on the Vectra computer and causes a program crash.

This selection is used to enter a tumor trace, thermocouple probe locations, a center to align them to the gantry center, and an edge point to find the correct orientation. When selected, the pain program will first check that the graphics tablet has been turned on. If it has not, a message will be displayed asking that it be turned on.

In the rare event that the pointer on the screen is stuck in a corner, regardless of the movement of the stylus, the graphics tablet did not initialize correctly. The remedy is to reboot this computer by pressing CRTL-ALT-DEL simultaneously and restarting the pain program. All tablet entries are on a 1=1 scale: one millimeter on the table equals one millimeter on the screen. This allows the transparency being traced to be held up over the computer screen to check for correctness. After entry the scale that the eateries are displayed is dictated by the screen scale described in the section on the ZOOM command. The orientation of the screen is a standard cartesian coordinate system with the origin on the lower left portion of the screen. Y increases up and X increases to the right. The graphics tablet is configured with the same coordinate system as the screen.

The first entry is the tumor trace. If a mistake is made and the user wishes to start entering the tumor trace over again, press the "SPACE BAR". At this stage in development, the tumor trace is only used for display and has no effect or meaning to the pain program except for display purposes. There are four colored buttons on the graphic tablet stylus that all act the same. The buttons are toggled with the upper left portion of the screen displaying the current state of the buttons as either TRACE OFF or TRACE ON. Thus, momentarily pressing one of the four buttons will change the state from ON to OFF or visa versa. The tumor trace section has two data filters to limit the amount of data input. The first filter requires that there must be at least 5 mm between data points. The second filter demands that the angle between consecutive data points must be less than 180 degrees. If the angle is more than 180 degrees, the computer will stop

accepting new points until the second condition is again satisfied. When the end point of the trace reaches within 10 mm of the start of the trace, the pain program will automatically connect the points and move onto the next stage.

The pain program will then prompt for the entry of the tumor trace center which will be used to align the tumor trace and thermocouple locations to the gantry scan center (see the warning below). Move the stylus to the desired center point and press one of the stylus buttons. Next, a point somewhere on the edge of the trace must be entered in the same manner. The edge point is used to rotate all information entered with the tablet to the same angle as the patient. The pain program then asks for a confirmation. Answering anything other than "Y" or "y" will allow the re-entry of the tumor trace, center, and edge point.

The pain program will now want the number of probes the user wishes to enter. The acceptable range is from 0 to 8. If the HP temperature computer program has been executed past the "Y" confirmation at the "Is all the data correct?" prompt, the pain program will have the correct number of probes to enter as the default. To except the default number of probes just press ENTER. While the pain program will accept a different number of probes, doing so will result in a "PROBE COUNT MISMATCH" warning when the first set of temperature readings is taken unless the HP temperature computer has been restarted with the new number of probes. If this mismatch warning occurs, the pain program will show the number of probes it is receiving and erase all the

previously entered traces, probe locations, and tumor center so that new ones can be entered. If the HP temperature computer has not run past this prompt the user will be required to supply the correct number of probes. Again, if this number does not match the number of probes received during the first reading the action described above will be taken and this section will have to be repeated. If the number of probes to be entered is zero the pain program will ask for a "Y" or "y" confirmation before continuing. If the last probe is a surface probe, respond with a "y" to the question "Ignore last probe". This has the same effect as using the VALIDATE TC command for all seven thermocouple of the last probe entered. Next, THE PROBES MUST BE ENTERED IN THE SAME ORDER AS THEY WERE (ARE TO BE) ENTERED IN THE HP TEMPERATURE COMPUTER. The tip of probe one is entered first- move the stylus to the desired location and depress a stylus button. Next, enter any point along the probe in the same manner as above that is at least 10 mm away from the tip point just entered. The pain program assumes that the probes are positioned in the X-Y plane and are 60 mm in length with seven sensors spaced 10 mm apart. Continue this process until all of the probes are entered. Pressing the SPACE BAR will start the probe entry process over. After the last probe is entered answering anything other than "Y" or "y" to the prompt will also start the process over.

WARNING: THE TUMOR CENTER POINT MUST NOW BE ALIGNED TO THE CORRESPONDING LOCATION ON THE PATIENT!!! After the location entry described above, the pain program will align the tumor/probe center with the current

gantry display center. If the gantry display center is not currently located at the center entered on the trace entry, the display would be spatially incorrect and misleading. Therefore, the user must first move the gantry to the edge point that was entered above and use the ENTER EDGE POINT menu option described below. Then when the scan starts, the program will determine the scan center which must align with the center entered above. The trace and thermocouple will not be displayed until both the edge point and center point are entered from the gantry position. When the first new center is established by either the MOVE CENTER command or automatically by the apple, the pain program will execute a ALIGN TUMOR TRACE command to align the centers. Therefore, the first scan of the gantry should be centered on the location on the patient indicated by the center entered in this section.

A.3.11 SCREEN TARGET 42.5˚C: hot key = "S".

This command is used to change the temperature at which the thermocouple temperatures displayed on the screen change from blue to red. A temperature displayed in blue indicates that the thermocouple is below the screen target and a red temperature means that the thermocouple is above the screen target. The screen target is completely separate from the temperature controller target. The screen target is only used for an informative display. To change the screen target up or down the "+" or "-" keys are used respectively. The screen target increments are 0.1 ˚C. The valid range is from 20 ˚C to 50 ˚C. If either limit is exceeded, the screen target will rollover to the other limit.

The default screen temperature is shown here as 42.5° C and will always reflect the current setting.

A.3.12 T/C VALIDATION: hot key = "V".

This command is used to prevent a thermocouple from being displayed and from being considered for use as input to the temperature controller. The pain program will prompt for the thermocouple to be ignored. The numbering scheme for the thermocouple are the same as for the HP temperature computer. Enter the two digit number or if the thermocouple number is less than 10 and only there is only one digit, enter the single digit and press ENTER. The pain program will then ask "IGNORE T/C X (Y/N)" (where X is the thermocouple number being considered). Responding with "Y" will have the effect of disabling the thermocouple. A "N" response will reverse a previous ignore command. This command should be used when a thermocouple is known to be broken, when a thermocouple is not in tumor, or the user just does not want a particular thermocouple to be used. When a thermocouple is ignored, the change is not seen on the screen display until the next temperature reading or until the screen is redrawn. Only the decimal points of a deactivated thermocouple are displayed.

A.3.13 ENTER EDGE POINT: hot key = "P"

This selection must be used after the traces are entered with the graphics tablet and before the scan starts. The gantry must also be aligned to the location that was entered with the ENTER TUMOR TRACE AN T/C option before selecting this item. Once selected the program will ask for confirmation to the location entered. The edge point can also be re-entered if the patient rotates his/her position. Patient movements in the X and Y direction should be corrected by the use of the move center command witch is done using the ALIGN TRACE command.

APPENDIX B: ORIGINAL PAIN ALGORITHM

The following algorithm describes the set of events for multiple pain button presses in the same approximate location or window. Two pain button presses are considered to be in the same window if the distance between them is less than the current window diameter. The program is capable of handling up to 300 (an arbitrary limit) presses and multiple independent windows. For excessive numbers of windows the speed of the program becomes hindered as more and more regions are established.

The action of the computer from pain button presses and the reasons behind those actions can be outlined in seven steps below and can be seen in Figure B1.

The overall goal of the algorithm used was to deliver as much power as possible to the patient without causing excessive pain. To this end, the patient tolerance for pain must be found. This is accomplished by the following set of predetermined actions to possible situations.

STEP ONE:

Upon the first press of the pain button a circle of operator selected diameter (from a default setting of 10 mm to a maximum of 98 mm) is established around the location of that the gantry was at the time the press (Figure B2). The ultrasound power to the transducers is immediately reduced to 0% while the gantry is inside of this window.

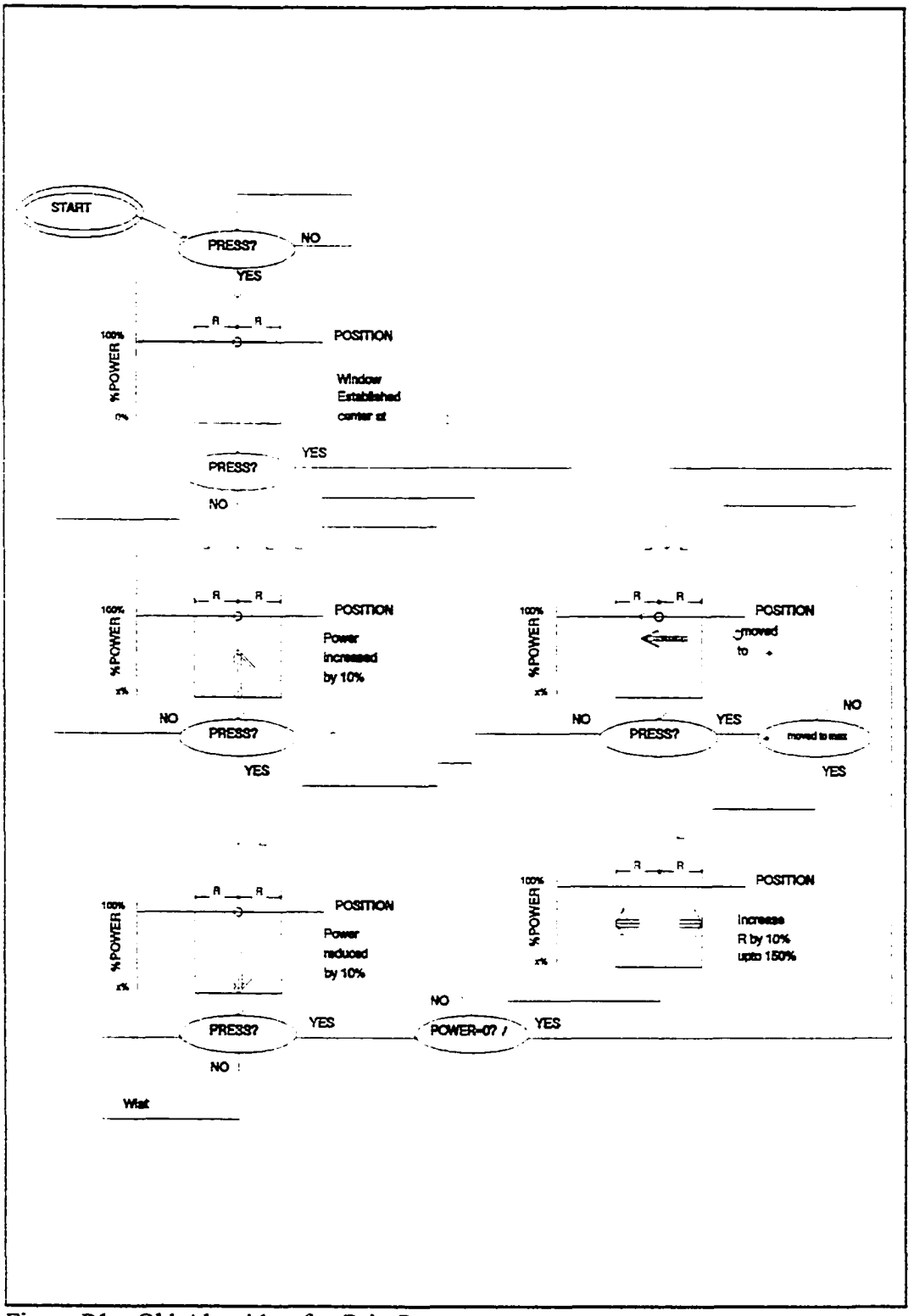

Figure B1. Old Algorithm for Pain Button.

STEP TWO:

During each subsequent pass through the window the power will increase by 10%. This is to see if the patient can tolerate more power (the goal is to deliver as much power as possible).

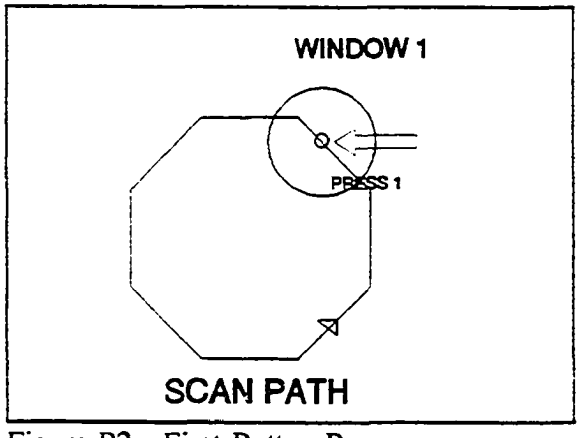

Figure B2. First Button Press.

STEP THREE:

If the power reaches 100% without any additional pain button presses, the window will be removed. The reason behind this action is that the patient was experiencing a one time pain. Or, thermal build up in the tissue or bone has occurred which should have been relieved by the temporary reduction in power to that area. Or, the press was an accident and should be ignored as it did not represent the patient's true condition. (A late modification to this step has been made so that the power inside of a window will not increase past 90%. Also, the windows are no longer removed)

STEP FOUR:

Additional presses inside the window will cause the power to be reduced by 10% from its previous value and be maintained at that value. This press is taken to indicate that the power was increased past the patients tolerance for pain in the window and the power should therefore be reduced. No additional power modifications will occur with each subsequent pass through the window as long as no additional pain button presses take place. If an additional press occurs while the power is being held at a fixed value, the program will lower the power by another 10% and hold it for future passes of the gantry through the window. This step will repeat for each press in the window until step five is reached.

STEP FIVE:

If a press occurs while the power is at 0%, The window is relocated back by one radius (Figure B3). This indicates that the patients reaction time was slow during the first press and the window needs to be moved back to try and cover the area that is actually experiencing the pain. The pain program then restarts the status of the window at step 2 in the hope that the actual location is now known and the power tolerance can be found.

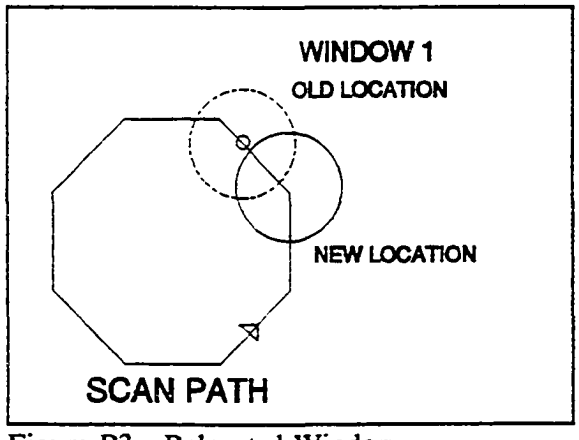

Figure B3. Relocated Window.

STEP SIX:

Step five is limited to three repetitions per window. After three, a button press inside a window with zero power will cause the window diameter to be increased by 2 mm in a last attempt to relieve the pain (Figure B4). The computer then restarts the window at step 2

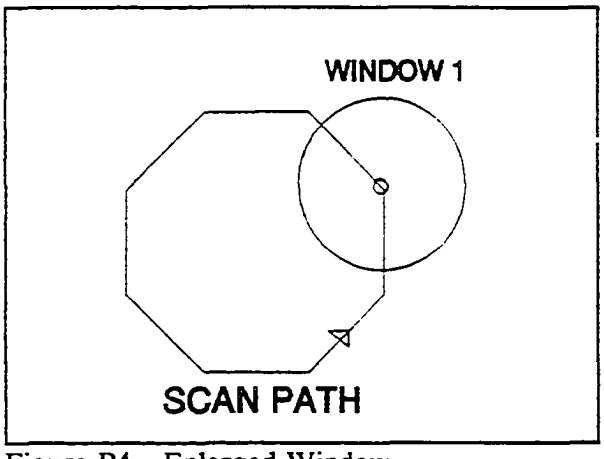

Figure B4. Enlarged Window.

STEP SEVEN:

Step six is only allowed to increase the window size to 150% of its original size, after which no further action is taken.

APPENDIX C: WIRING CONNECTIONS

VECTRA QS/20 2801 50 PIN IDC	GANTRY POTENIOMETERS 25 PIN DB FEMALE	SIGNAL NAME
1 a/d input ch0	1	X
2	25	GND
3 a/d input ch1	2	Y
4	25	GND
5 a/d input ch2	3	Z
6	25	GND
7 a/d input ch3	4	ROTATE
8	25	GND
9 a/d input ch4	5	TILT A/D
10	25	GND

Table C1. Connections Between the Gantry and Vectra.

VECTRA QS/20 2801 50 PIN IDC	DUTY CYCLE BOX 15 PIN DB FEMALE	SIGNAL NAME
38 bit 1/0	9	Button press
29 bit 0/1	10	reset bit
30 bit 0/2	11	safety
27	15	D-GND

Table C2. Connections Between the Vectra and Duty Cycle Box.

VECTRA QS/20 2801 50 PIN IDC	APPLE A/D CARD WIRE NUMBER	SIGNAL NAME
35 bit 0/6	3 ch2 yellow	center indicator
36 bit 0/7	1 ch0 black	inner/outer indicator

Table C3. Connections Between the Vectra and Apple.

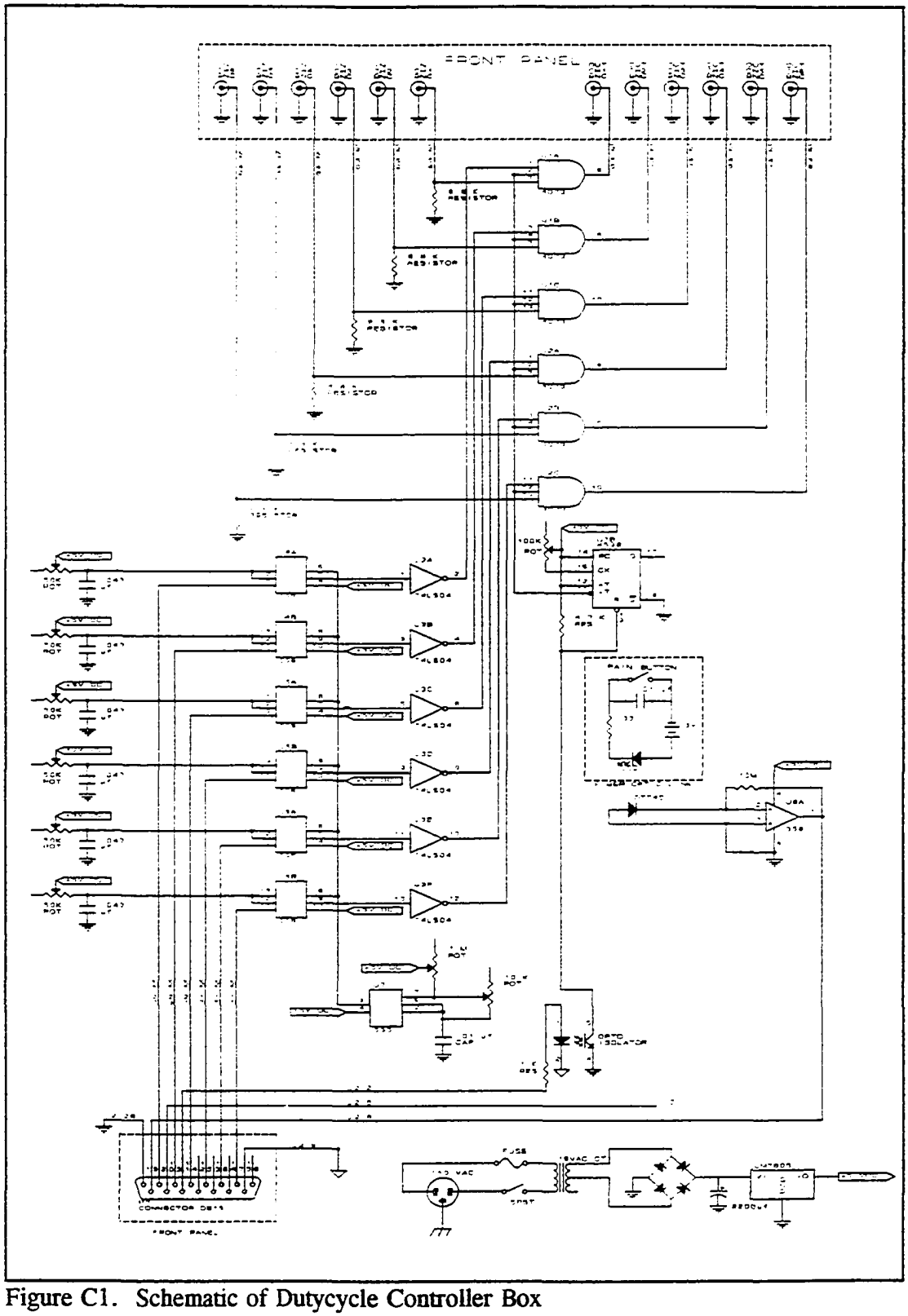

Figure C1. Schematic of Dutycycle Controller Box

APPENDIX D.0: GRAPHICS TABLET AND BOX CALIBRATION

D.1 ACCURACY OF THE TABLET

It was necessary to determine the accuracy with which data could be entered by the use of the tablet. To this end a short accuracy study was undertaken. The result of the study showed that data points could be entered within 0.2 mm (on average) with no edge effects or nonlinerarities.

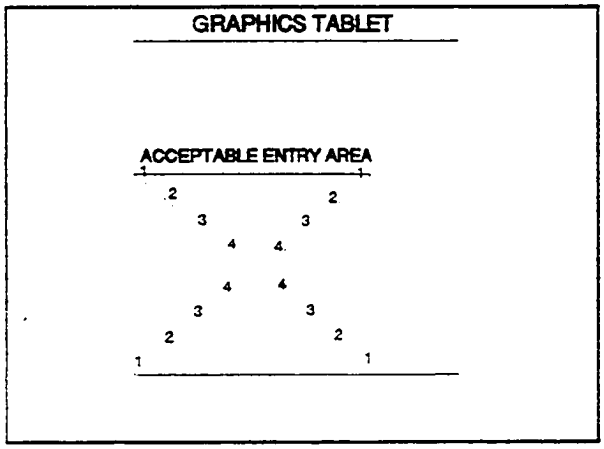

Figure D1. Test Pattern.

This result was obtained by entering the end points of sixteen radial line segments divided into four categories that covered the acceptable area for data entry for the pain program. D1 shows the orientation of the segments entered and how they were categorized. The entry of the segments was repeated five times with the results shown along with the standard deviation for each category in table 1.

Line Number	Line Length	Standard Deviation
1	21.01 mm	0.24
2	21.28 mm	0.23
3	21.00 mm	0.16
4	21.18 mm	0.20

Table D1. Graphics Tablet Test Results.

The true length of the lines was 21.2 mm. Since no trend can be seen in Table 1, it was concluded that no edge effects or nonlinearalities existed in the data. These results are consistent with the specification of the tablet which rate its accuracy at a maximum resolution of 40 lines per millimeter (0.025 mm as the smallest distinguishable stylus movement). The difference between the measured and specificated accuracy is attributed to operator entry error.

D.2 DUTY CYCLE BOX CALIBRATION

It is necessary to calibrate the timing constant of the mono shot timer so that the length of pulses are long enough to reach between the trigger pulses. The procedure to calibrate one of the channels on the duty cycle controller is as follows:

1. Connect the input to the channel being calibrated to TTL high.
2. Connect the output of that channel to an oscilloscope.
3. Set the output from the Data Translation 2817 D/A card to its lowest setting by outputing a digital value of zero using the PCLAB software.
4. Adjust the potentiometer located next to mono shot timer corresponding to the channel being calibrated until the output on the scope shows close to a 100% duty cycle.

It is very important that the duration of the output from the mono shot timer not be allowed to exceed the time between the trigger pulses. Doing so would yield unpredictable duty cycles.

After this adjustment, it is necessary to correlate the digital values to be sent to the Data Translation Card that are required to produce each desired duty cycle increment (0%, 1% 2% ... 99% 100%). This is done by connecting the channel to be adjusted in the same manner as specified above except the output needs to be connected to a meter that measures duty cycle (the screen of an oscilloscope can be used but the duty cycle measurements are not as accurate). Once the values are found for each channel, a polynomial needs to be found to allow the program to accurately interpolate between the data points (third order is sufficient). The coefficients for the polynomial are entered in the POSITION subroutine.

To change the frequency that the duty cycle controller operates, adjust the timing constant of the timer with the potentiometer located next to the free running 555 timer or by changing the capacitors located in the same area for different capacitor values to achieve the desired frequency (see the Figure 15 for wiring details). The specification sheet for the 555 timer contains a table that lists the required resistances and capacitances for assorted frequencies. After a frequency adjustment, it is mandatory that the above calibration procedure be followed for all channels to assure that the correct duty cycles are specified by the pain program.

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